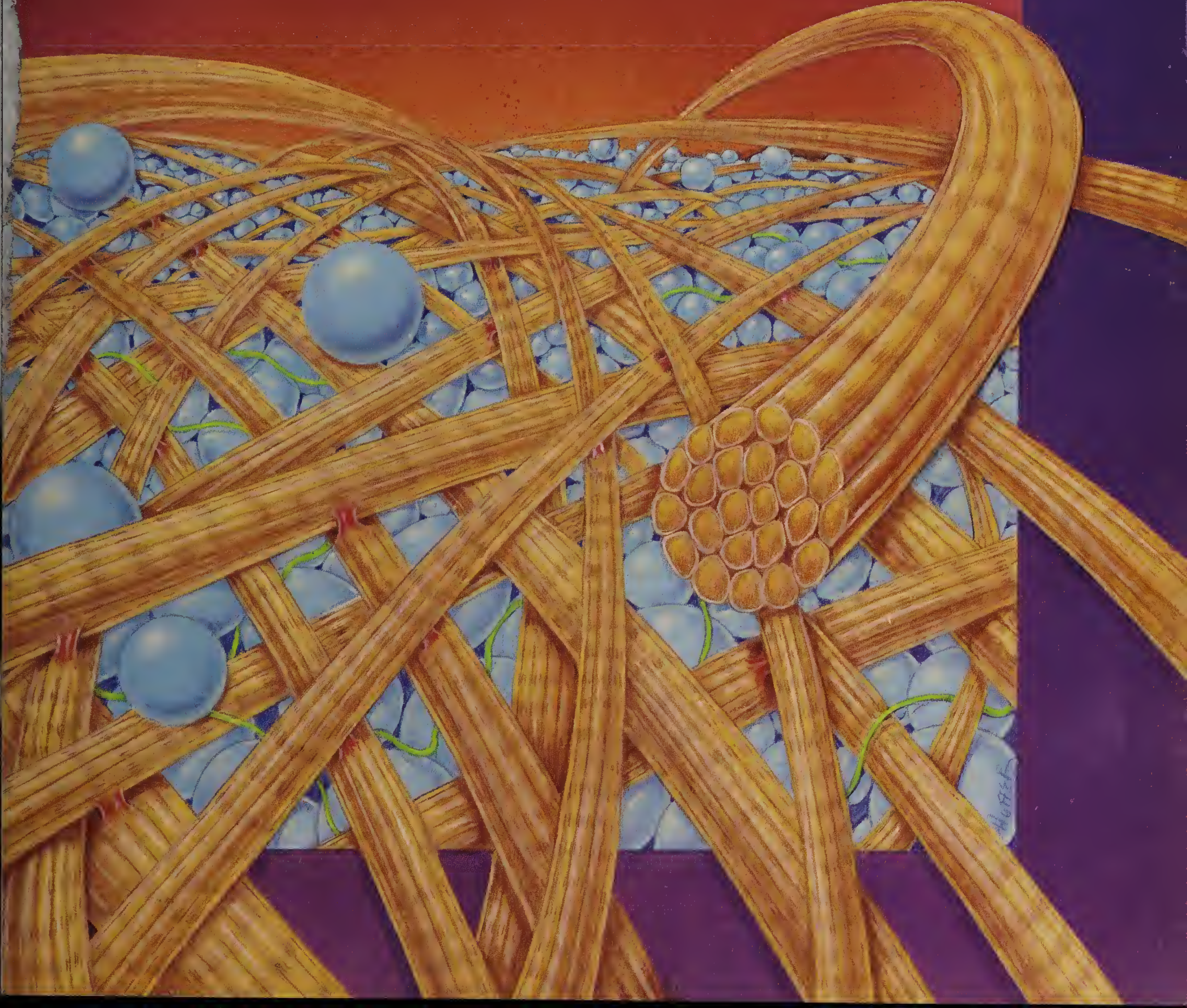
RUSH-PRESBYTERIAN-ST. LUKE'S MEDICAL CENTER

The Magazine

Summer 1988

ARTHRITIS:
Probing the Cause, Treating the Effects



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Proteoglycans escape from the collagen matrix,
the result of destructive forces at work in osteoarthritis.

ARTHRITIS:
Probing the Cause, Treating the Effects

By Mary-Ann Redeker

OSTEOARTHRITIS: A Little Understood Crippler

A snip. And then another. Destructive forces are at work within cartilage, breaking down its support system. The cartilage marshals its forces but has difficulty repairing the destruction fast enough. Small holes form in the surface layer and the forces go deeper, through the intricately structured cartilage layers to the bone. The process of osteoarthritis (OA) is underway.

If you live long enough, you will probably get osteoarthritis, the most common joint disorder. A large percentage of the population over 40 years shows some degree of osteoarthritic changes; more than five million of those suffer from severe disabilities.

Yet, little is known about this potential crippler. OA is the result of destruction of cartilage, a thin, milky-looking tissue covering the ends of the bones. But the exact cause and cure remain elusive. Once started, progression of OA is largely irreversible since the body lacks the capacity to appropriately repair cartilage.

OA can result in complete joint destruction, causing severe pain and deformity, or, in less severe cases, periodic inflammation, minor joint damage and mild discomfort. It can be found in one or two joints (localized) or in several (generalized).

For many years, it was believed that cartilage damage was the result of normal joint "wear and tear," which could be exacerbated by trauma, obesity or joint misalignment. Today, it is apparent that abnormal cartilage metabolism plays an important role in the cause and progression of osteoarthritis. Rush biochemists coined the term "chondrocytic chondrolysis" (the self-destruction of cartilage by chondrocytes or cartilage cells) to describe this process.

Until recently, there were no early detection tests for OA, and no evaluations to measure its progression. Since cartilage tissue does not contain nerves, three common symptoms of OA—joint pain, tenderness and limitation of movement—are detected late in the disease process.

"By the time a patient with OA shows up at the doctor's office, there has already been significant damage to the cartilage," says Klaus Kuettner, Ph.D., the John W. and Helen Watzek professor and chairman of biochemistry, and coordinating force behind the 13 Rush researchers involved in the SCOR grant research on osteoarthritis (see story on page 13). "As a short-term solution, halting the progression of the disease is the way to go. But ultimately you want to find a way to treat OA by encouraging the cartilage to repair itself."

Rush researchers hope to achieve both these ends through a continuum of research in osteoarthritis. On one end, developmental biologists and biochemists are working to understand better the function of normal cartilage and the disease processes; at the other, orthopedic surgeons are evaluating treatment options and surgical prostheses.

Scattered along this continuum are biochemists, rheumatologists, cell biologists, pathologists, anatomists and pharmacologists, searching for disease markers, a better understanding of age-related changes in cartilage and methods for early detection of osteoarthritis.

"When dealing with this disease, you can't operate in a vacuum. You need to pool knowledge from many different disciplines," Dr. Kuettner observes.

Sally Henriksen, R.P.T., director, physical therapy, Sheridan Road Hospital, demonstrates gait training.

The Role of Cartilage

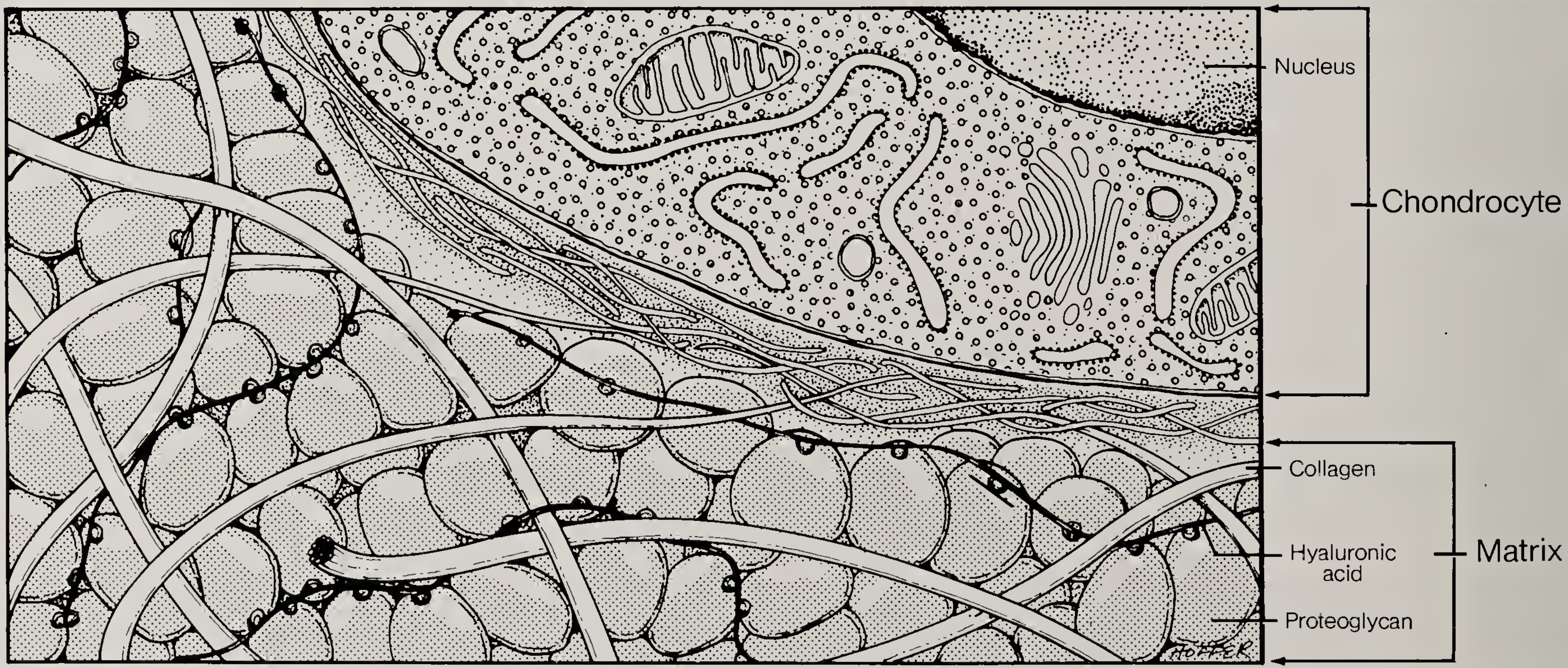
Joint cartilage serves as a cushion or shock absorber for the bones it covers. It allows the underlying bone to hold up over a lifetime of running, walking, sitting and standing. Cartilage maintains its form yet yields to compression and cushions the forces of impact, absorbing shock and protecting the more rigid underlying bone against mechanical damage. It functions as it does because of its structure: a few cells (chondrocytes) surrounded by vast areas of extracellular matrix.

Matrix is made up of proteoglycans and collagen. The proteoglycans, composed of many negatively charged sugars on a protein backbone, are attached to strings of hyaluronic acid (HA). Since identical charges repel each other and since proteoglycans are present in the tissue in a very high concentration, forced by the rigid collagen fiber network to stay close together, they try to get far away from each other by taking up water. This proteoglycan/HA configuration resembles a string of water balloons, trapped within and supporting the rigid structure of collagen and being compressed by the loading forces. During the process of motion, the water moves in and out of this structure.

Destruction occurs when enzymes come along and "snip off" the proteoglycan "balloons" from each strand of HA. The collagen loses its support, water enters the tissue and the fibers are crushed when the joint presses down on it, forming holes in the superficial layer of cartilage.

Cartilage is a self-contained system. Two finely balanced processes, anabolism (synthesis) and catabolism (breakdown), keep the inner workings (metabolism) of cartilage functioning normally. Until recently, OA was thought to stem from an imbalance of these two processes—too much "breakdown" and no synthesis. Scientists now know that both processes are elevated in OA, but they are not elevated with equal control.

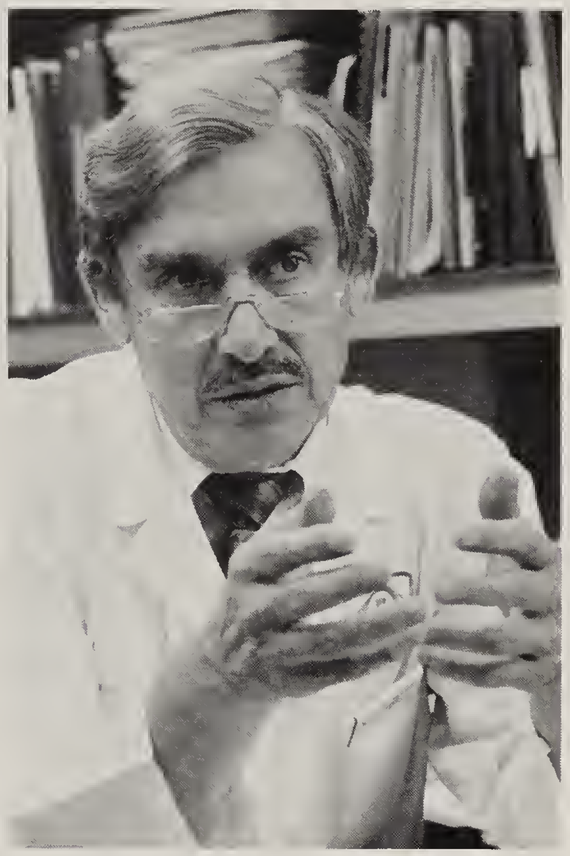
These discoveries have led researchers to hypothesize that OA



Chondrocyte with its matrix.

"...ultimately you want to find a way to treat OA by encouraging the cartilage to repair itself."

Klaus E. Kuettner, Ph.D.



Cartilage damage is usually significant by the time a patient with osteoarthritis sees a doctor, according to Klaus Kuettner, Ph.D., chairman of biochemistry.

may not be considered a degenerative disease. Degeneration implies a decrease in metabolism. Initially, there is no decrease in metabolism in OA, but actually, in its early stages, an increase, a tremendous attempt by the tissue to repair itself.

In order to investigate OA, chondrocytes (cartilage cells) had to be studied, with emphasis on uncovering ways in which chondrocytes could repair their surrounding matrix once OA begins. A difficulty immediately presented itself. In standard culture methods, chondrocytes rapidly lose their phenotype, or specific cell characteristics, and are unable to produce a cartilage-specific matrix.

However, building on culture methods initially developed by Dr. Kuettner, Margaret Aydelotte, Ph.D., assistant professor, biochemistry, adapted a system for growing chondrocytes within an artificial matrix (agarose) system, which is suitable for studying both anabolism and catabolism by these cells. This has given researchers a "living" cartilage model for long-term studies.

This agarose system is being used to study the effects of so-called mediators such as Interleukin I, which in diseased joints may induce chondrocytes to destroy their surrounding matrix, and specific drugs to see if they retard the OA process and if they produce any harmful effects on the tissue. "There are several drugs for the treatment of OA on the market in Europe," Dr. Aydelotte says, "but some of these are being withdrawn because of harmful side effects."

James Kimura, Ph.D., the CIBA-GEIGY professor of biochemistry and director of biochemical research in orthopedics, puts the problem of trying to encourage cartilage to repair itself this way: 1) cartilage does not repair itself very well and 2) we don't know why. In his laboratory, Dr. Kimura is working with two cell models to evaluate the biochemical events necessary to construct matrix with appropriate mechanical properties.

This biochemical research dovetails into a project which focuses on chondrocyte response to differences in their mechanical environment. Chondrocytes alter their metabolism in response to changes in loading. For example, when a joint is immobilized in a cast, over half the proteoglycans are lost over a few weeks through the "snipping off" process. But when the joint is remobilized and experiences a normal loading pattern, the cartilage returns to its normal state. Dr. Kimura and Thomas Andriacchi, Ph.D., the Claude N. Lambert, M.D.-Helen S. Thomson professor of orthopedic surgery, are interested in understanding how these loading forces affect the synthetic pattern of chondrocytes. They are currently developing a method which will allow scientists to describe the mechanical properties of the matrix being synthesized in culture.

"Once we have quantified in engineering terms what the matrix is like, we'd like to try to improve the quality of this matrix, using the system as both a measurement tool as well as a manipulative tool," Dr. Kimura says. "Dr. Aydelotte's artificial matrix model can be used to determine what agents can modulate what chondrocytes are doing. Our system can then assess the quality of agent-influenced matrix."

James M. Williams, Ph.D., assistant professor, anatomy, is also examining spontaneous repair of cartilage, studying the sequence of atrophied cartilage repair, using passive range-of-motion exercises.

Since OA is a multi-faceted disease with episodes of dormancy and inflammation, he has also developed a series of animal models to test specific theories and problems. In one model, chondrocytes are slightly damaged and their recovery is evaluated; in another, chondrocyte reaction and potential repair are studied in damaged matrix.

Explains Dr. Williams: "As anatomists, we're able to step back and get a broader view of the joint as a whole, which lends a more comprehensive understanding of the disease process."

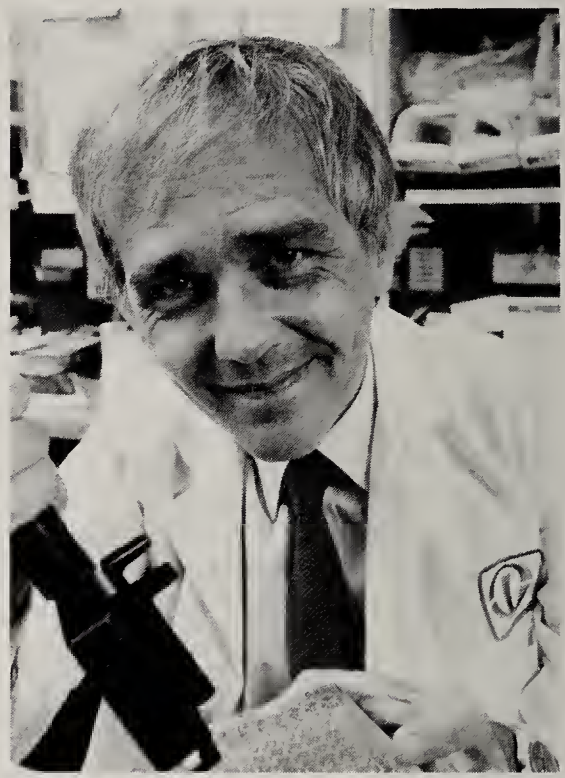
Tracking OA's Progress

The osteoarthritic process is a very complicated puzzle to piece together, once cartilage breakdown has begun. Eugene J-M.A. Thonar, Ph.D., principal investigator, William Noble Lane Medical Research Organization, and associate professor, biochemistry and internal medicine, found it easier to begin with very young cartilage cells to trace events throughout the life of these cells. Since chondrocytes don't die, the same cells are alive 30, 40, 50 years or more after they were originally formed.

In young cartilage, the proteoglycans make very large molecules; in old cartilage, the molecules are much smaller.

"Look at it this way. When you build a house wall with bricks, you're building the wall from scratch and would use large bricks," Dr. Thonar says. "When you repair the wall later on, it's easier to work with smaller bricks. But if you only have large bricks and small holes, you can't repair the wall. We think a similar problem occurs in osteoarthritis."

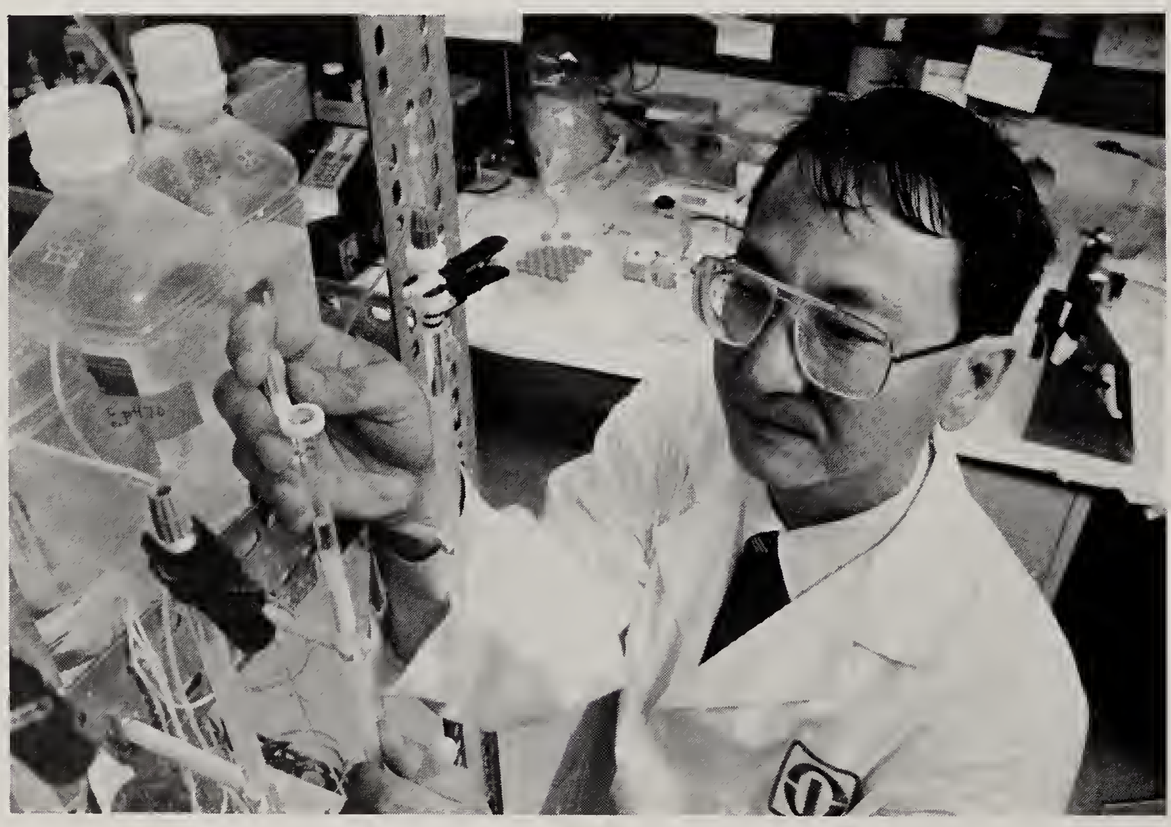
Young chondrocytes build matrix with large bricks. As they age, repair work is done with the small molecules. But in the case of OA, where scientists believe that the chondrocytes are remodulating to their original form, the chondrocytes revert to making large molecules or "big bricks," and the small holes formed in the superficial zone of the cartilage can't be repaired. The holes eventually become too large to accommodate any "bricks," causing matrix breakdown. The "snipped" molecules escape through these holes into the synovial fluid bathing the outer layer of cartilage, eventually reaching the circulation.



Eugene J-M.A. Thonar, Ph.D., has developed a serum assay for monitoring the presence of keratin sulfate in the blood.

It is this release of proteoglycan building blocks into the blood stream which has given Dr. Thonar one of the first OA markers. Proteoglycan core proteins have two major types of side chains, keratan sulfate (KS) and chondroitin sulfate. He has developed a patented serum assay to monitor KS levels in the blood.

KS is found almost exclusively in cartilage. When proteoglycans are being destroyed at an unusually fast rate, levels of KS rise in the blood. Studies have shown that when cartilage is destroyed chemically in one joint, there is a big increase in KS levels for two to three days, then a return to normal. It is the gradual rise in KS levels over a long period of time that signals problems in



How to encourage cartilage to repair itself is one of the problems James Kimura, Ph.D. is investigating.

> *"By picking up on problems early on through the KS assay, protective measures can be taken so that cartilage destruction is not exacerbated."*
>
> **Eugene J-M.A. Thonar, Ph.D.**

many joints.

"It is not inconceivable for a 40-year old with high metabolism to have the cartilage of a 70-year old," Dr. Thonar points out. "By picking up on problems early on through methods like the KS assay, protective measures can be taken so that cartilage destruction is not exacerbated."

The KS assay is particularly useful in tracking generalized OA, where the process is occurring in all the cartilage of the body. It also provides a non-invasive technique to monitor what's occurring within the joints.

Giles Campion, M.D., visiting lecturer/researcher in rheumatology and biochemistry from Bristol, England, working with Dr. Thonar and Rush rheumatologists, has obtained evidence that levels of serum keratan sulfate are elevated in about two-thirds of patients with OA. Importantly, levels appear to be highest in patients who have a familial history of generalized osteoarthritis. Retrospective studies are in progress to determine whether high levels of serum keratan sulfate actually precede the clinical manifestation of the disease. "This will help test the hypothesis that an abnormally high rate of cartilage proteoglycan catabolism (i.e. abnormally high KS level) is a predisposing factor to generalized osteoarthritis," explains Dr. Campion.

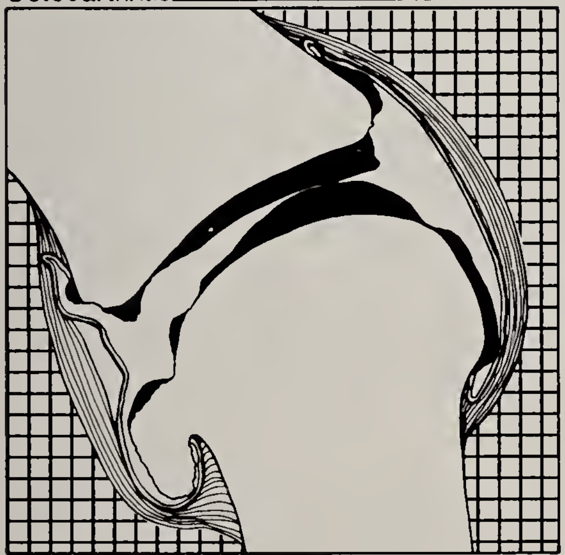
Researchers Warren Knudson, Ph.D., and Cheryl Knudson, Ph.D., are two of the team of Rush scientists involved in the SCOR grant project.

Rush researchers are just beginning to understand the basic functions of chondrocytes. In OA, for example, the chondrocytes are no longer making matrix correctly. "The cells make their matrix but then the matrix has to interact back with the cells to help regulate the state of differentiation," says Cheryl Knudson, Ph.D., assistant professor, biochemistry. "The mechanisms of cell matrix interactions are important in the initial formation of embryonic cartilage and the maintenance of healthy adult cartilage."

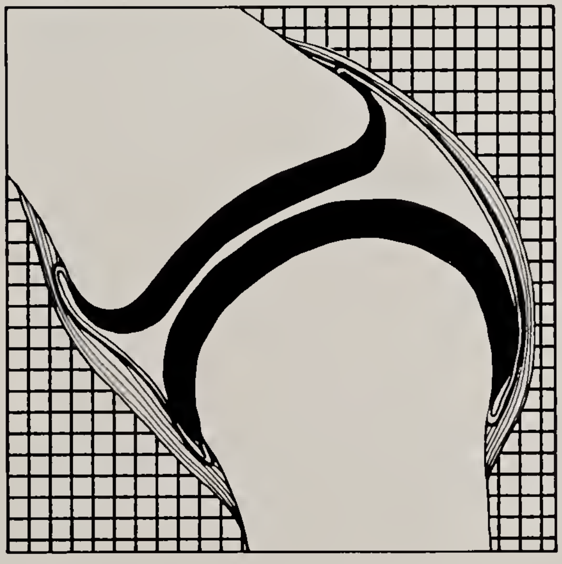
Researchers have also found profound physiological and morphological differences between chondrocytes in the different layers of cartilage.

Once defects develop in the superficial layer, the deeper tissue seems to deteriorate much faster. Superficial chondrocytes, with their unique metabolic properties, reside close to the synovial fluid within the thin layer of matrix they have created. Since this is the region of the tissue which is most directly exposed to agents (especially drugs) within the synovial fluid, it

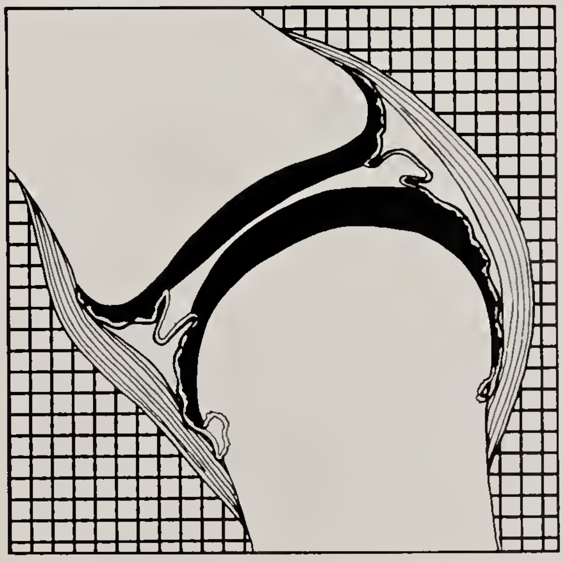
Osteoarthritis

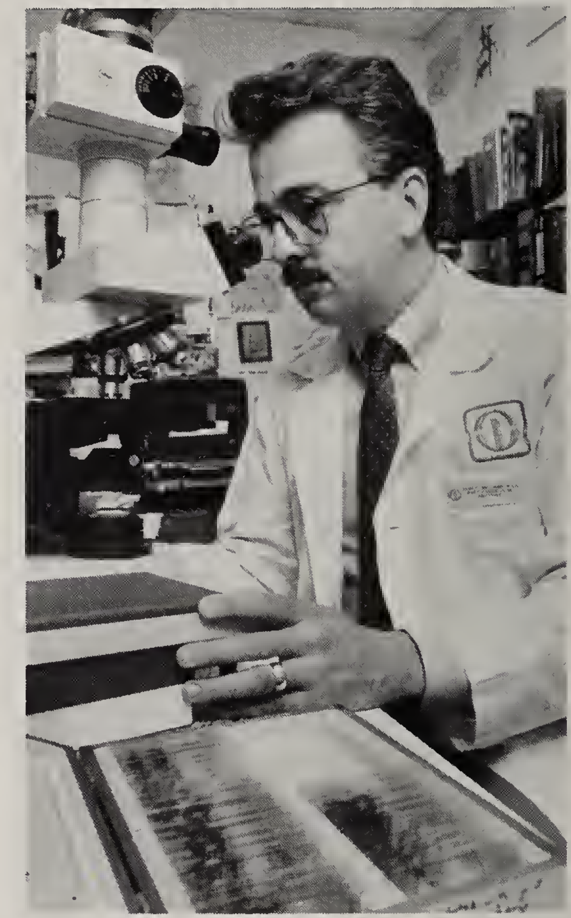


Normal Joint



Rheumatoid arthritis





James M. Williams, Ph.D., uses passive range of motion exercises in his study of the sequence of atrophied cartilage repair.

may play an important protective and/or regulatory role for the underlying cartilage. Understanding the different functions of chondrocytes in each of the layers will help researchers intervene at various stages of the disease.

"If we can catch osteoarthritis before the integrity of the superficial zone has been lost, we may be able to reverse the process of the disease," Dr. Aydelotte says.

Since cartilage lives in isolation, all protective mechanisms have to be present in cartilage tissue. Chondrocytes do not have cell-to-cell physical contact and all messages between cells must pass through the vast matrix which separates them.

Enzymes, synthesized during anabolism, in turn, act as catalysts for breakdown of the matrix. Theoretically, these enzymes should be destroying matrix on an on-going basis. But that doesn't happen. Dr. Kuettner's search for matrix enzyme inhibitors began years ago when he joined Rush. Many enzyme inhibitors were found, some which seemed to be tissue-specific and located within the matrix framework. Others, located within the circulation, seemed to be effective in regulating those enzymes secreted by leukocytes during the inflammatory process.

During the inflammatory process there is an infiltration of leukocytes into the joint space. Leukocytes use enzymes to clean up the debris of the inflammatory episode. The key destructive enzyme of the leukocyte is elastase, which can destroy practically all components of the extracellular matrix.

What remains at question is why, under normal, non-disease conditions or even during an inflammatory episode in OA, is leukocyte elastase not destroying cartilage? Dr. Kuettner and his German colleagues at Hoechst A.G. Pharmaceutical Corporation found an inhibitor in cartilage which seems to control the action of elastase. They are testing the possible application of this inhibitor in the regulation of cartilage degradation.

While Rush investigations have led to a more complete picture of the biochemical processes at work in normal and OA cartilage, its partnerships with industry, such as Hoechst and CIBA-GEIGY, U.S.A., establish a concentrated effort to develop paths of disease intervention.

"The 1990s will see an increased interest in the study of diseases that cripple a substantial portion of our society, since they are directly responsible for lost days of work and, therefore, a drain of society's resources," Dr. Kuettner says. "Special emphasis on understanding the etiology of these diseases and the development of therapeutic tools to arrest them is only a question of time."

Margaret Aydelotte, Ph.D., has adapted an artificial matrix system for growing chondrocytes, providing researchers with a "living model."

"Because of the complexities and unknowns surrounding RA, research and treatment at Rush are multidisciplinary.

Thomas Schnitzer, M.D., Ph.D.

RHEUMATOID ARTHRITIS: Battling Invaders

"Having the flu all the time and toothache in every joint," is how patients frequently describe rheumatoid arthritis (RA), the most common inflammatory disease of the joints. RA is most prevalent in 30- to 50-year-old women. Unlike OA, which develops slowly over a period of years, RA can flare up and cause damage in a matter of months.

RA is a systemic disease and may involve lungs, heart and nervous system, as well as joints. Damage to the joints is caused by invaders, the inflamed and invading synovial joint lining cells. The damage is comparable to cancer cell destruction of tissue. Due to the inflammation, the joint linings gradually begin to enlarge and secrete destructive enzymes into the joint space. When this becomes severe, the joint is damaged. Tendons and bursae, which lie over the bone, are involved, producing severe deformity.

Its cause remains unknown. A current belief is that RA is an autoimmune disease in which the body starts to attack itself. One of the hallmarks of the disease is a particular type of blood protein called the rheumatoid factor. Researchers believe that this autoantibody causes immune cell clusters to form which circulate throughout the body and are deposited in joints and other tissues, giving rise to inflammation. Precisely what causes the formation of these autoantibodies remains a mystery. Many researchers believe that it is a combination of genetic susceptibility coupled with an environmental trigger such as a viral infection that causes rheumatoid arthritis.

A definitive cure also remains elusive. Some treatments respond to symptoms, such as anti-inflammatory medications and pain killers; others, to the disturbances of the immune system and to joint protection (splints) and repair (prostheses).

"Rheumatologists are often the entry point into the health care system for the patient with joint problems. Therefore, they have to differentiate among many different diseases and make decisions about treatment," says Thomas Schnitzer, M.D., Ph.D., the Willard L. Wood, M.D., professor and director, Section of Rheumatology. "Because of the complexity and unknowns surrounding RA, research and treatment at Rush are multidisciplinary." Dr. Schnitzer came to Rush three years ago to expand and enhance research and treatment programs in rheumatology.

A major part of the clinical and basic research program in the Section of Rheumatology, coordinated with the Departments of Biochemistry and Orthopedic Surgery, focuses on a better understanding and more effective treatments for both OA and RA.

In patients with OA, rheumatologist-scientists have worked closely with Dr. Thonar to establish and evaluate the effectiveness of serum markers for cartilage degradation in OA and RA. "The ability to do a blood test to help rheumatologists get a better handle on the extent and severity of the joint disease will be extremely important and useful," Dr. Schnitzer says.

In other studies, researchers are evaluating the commonly used drugs for joint pain, especially the non-steroidal anti-inflammatory agents, to determine if they have any direct effect on the health of cartilage.

Further studies are also underway to determine if these drugs, when given to patients with painful knees, will have a significant effect on the way people walk. Using the Medical Center's Gait Analysis Laboratory in the John L. and Beatrice Keeshin Human Motion Research Laboratories, directed by Dr. Andriacchi, researchers are looking to detect small changes that may not even be able to be felt by patients. This research should lead to a better understanding of how these drugs work and a better selection of appropriate treatments.

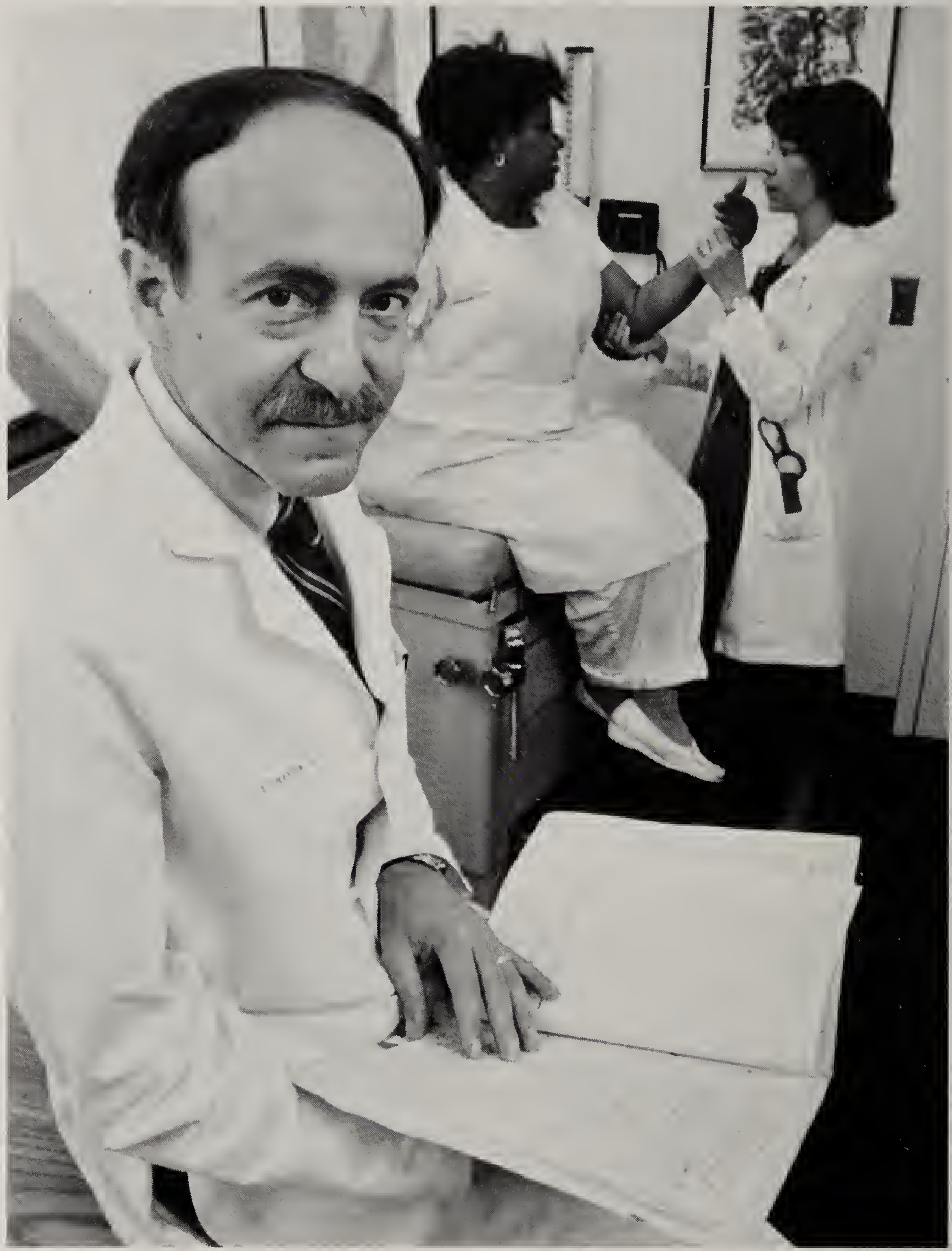
Not only are rheumatologists doing research in OA, but there is exciting new work in the area of rheumatoid arthritis aimed at directly treating the disease itself as well as helping relieve some of its side effects. Despite a number of powerful medications for patients with advanced rheumatoid arthritis, there is still no effective treatment to halt the progress of RA in more than half the patients treated. New drugs are being tested at Rush, as well as some older drugs that are now used in patients with RA for the first time.

Since RA is associated with an overactivity of the immune system, drugs inhibiting this system are being investigated. Cyclosporine, the drug that revolutionized transplant surgery, is being evaluated in a study with the Mayo Clinic and Sandoz, Inc., for the treatment of patients with advanced RA. Initial studies have shown remarkable efficacy; new studies will attempt to use lower doses to prevent some of the side effects of this drug.

For patients with less severe RA, more traditional treatments, such as gold, are being examined again, this time using an oral preparation rather than subjecting patients to weekly injections.

Some RA patients are troubled with anemias, an underproduction of red blood cells. In collaboration with Walter Fried, M.D., professor, internal medicine, Rush rheumatologists are using a product of modern biotechnology, human recombinant erythropoiten (a naturally occurring hormone which triggers red blood cell production) to see if it will increase red blood cell counts in patients with RA, making them feel less tired and more productive.

Because of its activity in studies such as these, the Section of Rheumatology has been awarded a Clinical Research Center grant from the Arthritis Foundation to help support further efforts to investigate the causes and treatment of joint diseases.



Thomas Schnitzer, M.D., Ph.D., conducts an examination of a patient with rheumatoid arthritis, a condition he says is surrounded with complexity and unknowns.

"We've found that patients who seek help early don't have as many problems as those who wait."

Richard Harvey, M.D.

TREATING THE EFFECTS

While the search for the cause and a cure for osteo and rheumatoid arthritis continues, rehabilitation specialists and orthopedic surgeons are refining and improving current treatments and therapies.

To date, pharmaceutical intervention, rehabilitation therapies, and, in very severe cases, surgery, are the main forms of pain relief treatment available to the patients with arthritis.

Richard Harvey, M.D., professor and chairman, physical medicine and rehabilitation, heads a service particularly geared to patients with joint problems. This service, in place for several years at Marianjoy Rehabilitation Center, a Medical Center network hospital, and at the Medical Center main campus, includes evaluation and treatment components. A multidisciplinary team—rheumatologists, physiatrists, orthopedic surgeons, orthotists, occupational and physical therapists, rehabilitation nurse specialists, psychologists, and vocational and work counselors—get involved with the patient's evaluation and treatment.

The question throughout the evaluation process is: what is the potential for reducing the effects of the disease? Rheumatologists focus on medical management—drug and treatment benefits; if the progression is severe, orthopedic surgeons are called in to discuss surgical therapies. If there is no potential for reducing the problems either medically or surgically, a physical rehabilitation program is initiated.

Muscle strengthening, heat therapies, orthotic devices to protect the joint and assistive devices are some of the common, traditional treatments for arthritis. Exercises help reduce wear and tear on the joints by strengthening muscles surrounding the joints. Pain is controlled through electrostimulation, exercise and heat therapy, with a de-emphasis on medications.

A new program at Marianjoy is the work evaluation system. "We try to find new ways to do the same job," Dr. Harvey says. "Fatigue is a common problem for patients with rheumatoid arthritis, because so much energy is used to battle inflammation and rebuild tissue. All that may be needed is a 'flex time' work schedule to accommodate for this. However, if joint involvement is severe enough, additional considerations such as assistive devices and different modes of transportation to and from work may have to be incorporated into the vocational treatment program."

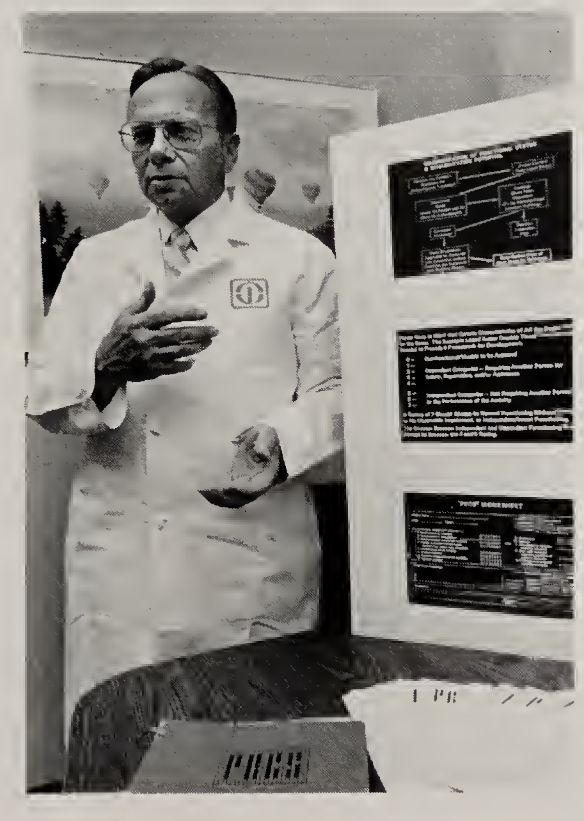
Once a method has been found to work around problems, a job-simulated situation is created in the treatment center. The work evaluation team goes to the patient's workplace and video tapes the environment to ensure that the compensatory methods developed in the treatment center do not conflict with the job setting. Repetitious "work hardening" exercises improve work tolerance.

If a patient can't return to the same job, other job training opportunities are explored. Through vocational counseling and a computerized listing of jobs and their characteristics. Patients are matched to appropriate jobs and a retraining program is begun.

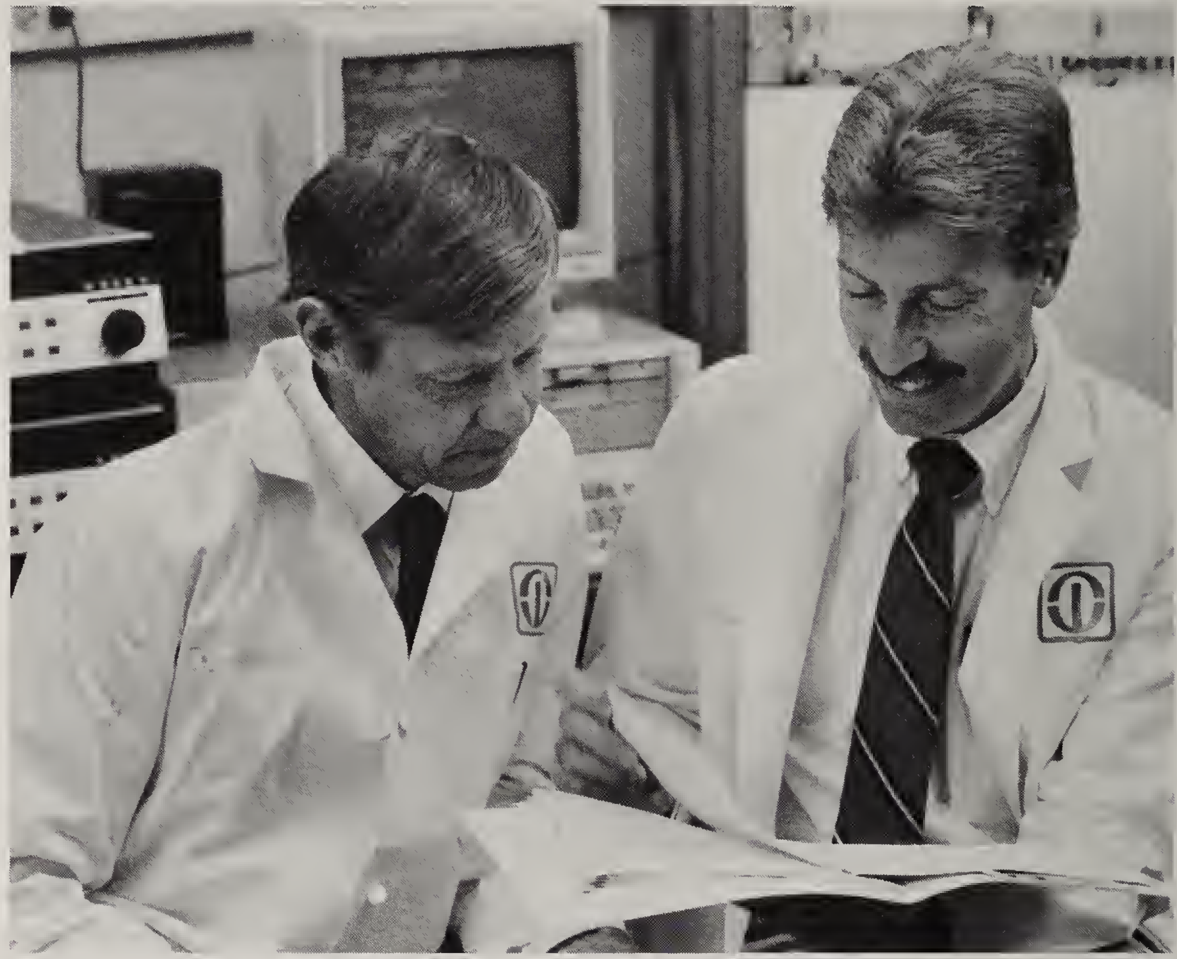
Rehabilitation nurse specialists, physical and occupational therapists and dietitians form a multidisciplinary team which concentrates on patient education (booklets, videos), comfort (splints to protect joints, range of motion exercises to strengthen limbs) and daily function (adaptive aids and assistive devices).

Evaluation, treatment and education programs for arthritics are also available at the Medical Center's Arthritis Centers at Sheridan Road Hospital and Rush North Shore Medical Center. At these centers, support groups fill a void for patients with arthritis. The monthly support groups are small to give patients a chance to share problems and offer emotional support.

"They learn from each other and



Richard Harvey, M.D., heads up a rehabilitation program geared to help patients with joint problems.



In a joint effort, Gunnar Andersson, M.D., Ph.D., (left) and Thomas Andriacchi, Ph.D., are analyzing the functional aspects of prosthesis procedures.

from us," says clinical coordinator Mary Ann Haag, R.N. Education rises out of problems. Questions about nutrition, for example, resulted in the group's meeting with a clinical nutritionist; a physical therapist discussed ways to get up after a fall.

"I think early intervention is the key to a successful rehabilitation program," Dr. Harvey says. "We've found that the patients who seek help early don't have as many problems as those who wait.

"The main thrust of all our programs is to *not* aggravate the arthritic process. We like to have our patients maintain their current level of functioning, but sometimes this isn't possible because of the course of the disease."

Joint prostheses have been one of the single greatest advances in the treatment of patients with severe, debilitating arthritis. "Implantation of a prosthesis will greatly reduce pain," says Gunnar Andersson, M.D., Ph.D., professor, orthopedic surgery. "But we don't know in detail how the different prostheses and different types of operations affect function."

Joint research is a many-faceted approach at Rush's Department of Orthopedic Surgery (see *The Magazine,* Spring 1984). Some orthopedic surgeon-scientists are analyzing the pros and cons of cement versus cementless fixation; others, the type of material used in

Education is an important aspect of a patient's treatment program. Here, Louise Nora, R.N., uses a model and educational materials to describe a procedure.

the prosthesis. The Medical Center's Gait Analysis Laboratory uses sophisticated equipment to measure motion and is integral to the study of design aspects of this research. Patients are studied when they walk on a level surface, go up and down stairs and get in and out of chairs.

Over the years, Rush scientists have amassed information from studies of patients who have had various types of prosthesis procedures. "But until now we haven't analyzed systematically the functional aspects of the procedures," Dr. Andersson says.

Some patients with newer, cementless designs have an unexplained minor limp which was not observed in patients with prostheses fixed with cement. Differences in stress transfer between cementless fixation (metal to bone) and cement fixation (metal to cement to bone) may be a factor in explaining the limp. Preliminary testing has indicated that minute variations in the placement of the prosthesis can substantially change the biomechanics of the gait. This is the thrust of this aspect of the SCOR research: to better understand the relationship between implant design, joint mechanics and patient function.

What Rush physicians and scientists are learning about arthritis in the petri dish and the laboratory, through industry-based cooperative programs and in progressive treatment settings is affecting the treatment of patients today. "It's our moral justification for being here," states Dr. Kuettner, who insists that all his researchers have a clinical associate. "What we learn and develop must feed back into the patient."

Until recently, 85 percent of all funds allocated to arthritis research supported studies on rheumatoid arthritis, which affects only one to two percent of the population.

In 1987, Rush-Presbyterian-St. Luke's was the recipient of one of only three Congressionally mandated, five-year SCOR (Specialized Center of Research) grants, awarded nationwide in the area of osteoarthritis research by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, a component of the National Institutes of Health.

The SCOR grant represents a culmination of research efforts by the Connective Tissue Group. The group, formed eight years ago by Dr. Kuettner, brings together the expertise of scientists and physicians from many departments within the Medical Center to foster collaborative efforts in basic and clinical osteoarthritis research.

The $3.5 million Rush SCOR grant in OA consists of five projects (discussed in these pages) and three supporting core facilities. Thirteen researchers, representing five academic departments, are involved in the projects. They are:

- *Klaus E. Kuettner, Ph.D., program director; the John W. and Helen H. Watzek professor and chairman of biochemistry; professor, orthopedic surgery.*
- *Gunnar Andersson, M.D., Ph.D., professor, orthopedic surgery.*
- *Thomas Andriacchi, Ph.D., the Claude N. Lambert, M.D.-Helen S. Thomson professor of orthopedic surgery.*
- *Margaret Aydelotte, Ph.D., assistant professor, biochemistry.*
- *Jorge O. Galante, M.D., the William A. Hark, M.D.-Susanne G. Swift professor and chairman of orthopedic surgery.*
- *James Kimura, Ph.D., the CIBA-GEIGY professor of biochemistry; associate professor, orthopedic surgery.*
- *Cheryl Knudson, Ph.D., assistant professor, biochemistry.*
- *Warren Knudson, Ph.D., assistant professor, biochemistry.*
- *Jerome R. Kuszak, Ph.D., associate professor, pathology.*
- *Thomas Schmid, Ph.D., assistant professor, biochemistry.*
- *Thomas Schnitzer, M.D., Ph.D., the Willard L. Wood, M.D., professor and director, Section of Rheumatology.*
- *Eugene J-M.A. Thonar, Ph.D., principal investigator, William Noble Lane Medical Research Organization, and associate professor, biochemistry and internal medicine.*
- *James M. Williams, Ph.D., assistant professor, anatomy.*

Leadership Committees bring together community leaders who work with special programs throughout the Medical Center. So far there are 10 designed by departmental interest, including orthopedic surgery, obstetrics and gynecology and multiple sclerosis. Trustee Donald Nordlund will act as chairman of the Leadership Committee for Arthritis.

Nurses Don't Realize How Valuable They Are...

In 1987, Kathleen G. Andreoli, D.S.N., came to the Medical Center as vice president for nursing affairs and dean of the College of Nursing of Rush University. An experienced nurse administrator, Dr. Andreoli shared her thoughts on present dilemmas in nursing and on its future.

Q: *We hear a lot about the shortage of nurses, but there's also a decline in the number of inpatients in hospitals. So how real is the shortage?*

ANDREOLI: When I was doing staff nursing many years ago, we would have patients who had been on the unit for extended periods, like one to two months. They would be rehabilitating in the hospital. This doesn't happen now, which means that those who are in the hospital are often intensely ill. As the acuity rate has gone up, the number of patients a nurse can care for has gone down. Where once we could assign ten patients, or eight, to one nurse, we're now lucky if we can assign two in areas like medical intensive care, or in pediatric intensive care where it is often one on one.

Not only has the acuity of the patient increased, so has the technology used to take care of the patient. That means we not only need more nurses, they have to be better educated than they were in the past in order to manage the technology.

Q: *Is the fact that nurses are more educated contributing to the shortage? Are they moving away from the bedside?*

ANDREOLI: I don't think so. A recent study, for example, has shown that there is a higher retention rate for nurses with master's degrees. Job satisfaction comes from the realization of a job well done, from a feeling of proficiency and contribution, the confidence to practice with certainty, to exercise a certain amount of autonomy, and to see things turn out well because you had the skills and can ask the right kind of questions. This comes with education and understanding.

Q: *Is salary contributing to the nursing shortage?*

ANDREOLI: There are several reasons why people won't go into nursing. One is low pay. Historically nurses have gotten low pay; how-

> *"Altruism is very important. The skilled altruistic candidate is the one who is going to do the best by the bedside. When you're sick, that's what you want... I know that's what I want!"*
>
> **Kathleen G. Andreoli, D.S.N.**

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ever, times are changing. Rush stands out because we pay the highest salaries in Chicago. Nationally we're probably among the top three medical institutions in salary. But, remember, there are 1.7 million practicing nurses; salary scale is not consistent around the country, and three institutions don't make that much of a dent nationwide. The wage issue is going to change; large academic medical centers across the country are taking the lead. But it is going to take a long time before others follow.

Someone asked me the other day that if we pay the highest salaries in Chicago how come all the nurses in the city aren't working at Rush. It is a matter of job satisfaction, which is an intrinsic motivator. Extrinsic factors, like salary, have less influence on job choice. The fact that people you work with like and respect you and you like and respect them, that your patients respect you and that you have an important position in a professional setting—that's what makes nurses stay. People use salary as a big issue (and it is important). The fact that all the nurses in Chicago are *not* standing in line to work here says they are satisfied where they are. Money is not everything.

On the other hand, from a monetary viewpoint, nurses just don't realize how valuable they are to a hospital, not only in service but in dollars and cents. I think you can say generally that every nurse employed by a hospital the size of Presbyterian-St Luke's gives the hospital the opportunity to earn the dollars necessary to meet its projected patient day budget. But what would happen if a hospital lost 100, 200 or 300 nurses? If physicians wanted patients to go into the hospital, it might not be able to admit them. That could mean the patients would go to other physicians. If the hospital couldn't admit patients, it would mean its beds would not be filled and it might go out of business. Now physicians don't want to lose patients and hospitals don't want to go out of business. There is a way to solve this—provide employment incentives via a professional environment reflecting a professional salary, professional nursing staff organization, primary nursing, levels of practice and nursing administration in charge of nursing.

Q: *Do you see an end to the shortage and, if not, what will happen?*

ANDREOLI: I don't see an end for the next ten years. What is eventually going to happen nationally is what we are doing now at Rush. We are investing in recruiting. The health industry has got to get intensely involved in recruiting people into nursing and in changing the image of nursing so it can attract women, men, minorities and second career people. We cannot take it for granted anymore that people want to become nurses. There is too much competition. What hasn't happened is that hospital administrators and physicians who are most frustrated by the shortage of nurses haven't given of themselves to correct the shortage, to resolve it. Nurses are not always successful in recruiting people into nursing, because nurses cannot demystify the myths. Physicians and hospital administrators must also get involved.

In the meantime we've got a

10-year period in which we must make do with our current work force of nurses. We are trying to make our nurses more efficient by giving them as much time-saving technology as possible, such as computer systems for measuring clinical signs, scheduling and managing patient records. We are also embarking on a program to test the feasibility of health workers on the unit who will be under the direction of the nurses. This technical person, called a unit assistant, will assist the nurses in activities not directly related to hands-on nursing.

Q: *Do you think that nursing education will change because you will be recruiting a different kind of student?*

ANDREOLI: Nursing education continues to change, depending on the trends of the day. Our curriculum is modified in response to the expansion of biomedical scientific knowledge and technology, just like any other health-related curriculum. I said earlier that nursing has become highly sophisticated and highly technical in the practice setting. Our trend-responsive College of Nursing has inaugurated a doctor of nursing (N.D.) degree program for the advanced clinical practitioner.

At Rush we place a high value on education. Eighty-five per cent of our staff nurses are baccalaureate prepared. Few places can say that. Many of the remaining 15 percent are enrolled in degree programs through our tuition reimbursement program.

Q: *Will there ever come a time when the majority of nurses will have the baccalaureate or higher degree?*

ANDREOLI: The largest health profession is nursing and the largest variation in preparation is in nursing. Historically, to be licensed you could complete a two-year community degree program, a three-year diploma program, or a four-year baccalaureate program. Now we have the master's level for the clinical specialist and advanced practitioner-researcher-administrator programs at the doctoral level. In contrast, those preparing for other health professions—medicine, dentistry, physical therapy, medical technology, for example—enter a more ordered educational program.

At times nursing is its own worst enemy. It has to unify on the issues of entry into practice and credentialing. Since our numbers are so enormous and so varied in education, it is going to take a long time to get unity on the issue of preparation.

Q: *What do you consider the most important issues in health care?*

ANDREOLI: The nursing shortage and health policy. In our economy everything is dollar-driven. Medicine is a business; hospitals are a business. What will make the difference in terms of the survival of quality health care is whether health care will be available and accessible. Accessibility will come from the way the laws of the land are written. The Federal Government has made an incredible impact on delivery of health care services—on whether or not they can be delivered and paid for. But for health care to be available there must be professionals to deliver it—and that's where nurses come in. We can have laws that make health care accessible, but if the professionals aren't there to give it people won't get the care that can be paid for.

Q: *Are there going to be new forms of practice opportunities for nurses, beyond bedside care?*

ANDREOLI: Health care is being de-institutionalized right now. The current ratio of 60 percent of the nation's nurses in hospitals and 40 percent out of the hospital will reverse. The career choices for nurses are numerous, especially in areas of outpatient care. Patients are now at home with ventilators, with home infusion, with dialysis; nurses are monitoring these patients, caring for them. In home health care "you ain't seen nothing yet." Another area is long-term care of the elderly which until now has been virtually ignored. The laws are going to be changing in this regard because more voters are moving into the higher age levels. State requirements will be changing for nursing homes and other long-term care facilities where an R.N. 24 hours a day is not necessarily a rule now, and educational requirements for the care of the elderly will be upgraded. Wellness is becoming important and nurses will be working in this area in schools and businesses.

Q: *Will this help recruitment into the profession?*

ANDREOLI: I suppose some people might be attracted if you told them they could be a vice president for nursing at a major academic medical center or that they would have an important title in business. But you have to start out with what people recognize about nursing. I went into nursing because I wanted to take care of sick people. Those are the kinds of people I would like to have come into nursing, not those who aspire to make a great deal of money or to rub shoulders with important people. Altruism is very important. The skilled altruistic candidate is the one who is going to do the best by the bedside. When you're sick, that's what you want.... I know that's what I want!

New Roles in Nursing: MD/RN The Joint Practice

What happens when a patient calls the doctor to ask a question and discovers it's the nurse who will be providing the answer?

"Some older patients have a problem with a nurse having so much authority and not being by the bedside," says Patty Piasecki, M.S., R.N., "but once they understand my role most appreciate what it provides them."

Piasecki's special "role" is one that is fairly new to nursing. She is in joint practice with Steven Gitelis, M.D., an orthopedic oncologist and assistant attending surgeon at the Medical Center. Piasecki and Gitelis operate as a team serving tumor patients needing bone transplants and orthopedic patients requiring total joint replacements. They share an office with adjoining desks in the Medical Center's professional building, an arrangement Piasecki says helps communication because they can each hear what the other is saying to patients over the phone. They often do patient rounds together and they confer on many aspects of patient care.

Although physician-nurse joint practices are not widespread, a number are active at the Medical Center. For patients, the joint practice provides for both their medical and nursing needs, two different but necessary elements of care. There is, however, no set pattern for what the nurse does in this relationship. Each practice is different, Piasecki says.

Her major responsibilities are teaching and patient (including family) support. When Dr. Gitelis is in surgery, Piasecki is the one who is available to patients, Sometimes, she says, she is on the phone a good part of her day.

"I have a long-term relationship with our patients. It begins the first day they come to us and continues through their hospitalization and aftercare."

This availability is a bonus for patients. If a tumor patient needs to be seen right away and Dr. Gitelis is in surgery, Piasecki will start the work-up and arrange for the necessary tests. Often a first-time patient will be seen initially by Piasecki, who will take the history and do the physical. Dr. Gitelis will then go over the highlights with the patient. Piasecki admits that patients not familiar with a joint practice often mistake her for a medical resident.

"I see all our patients in the hospital on a daily basis, either with Dr. Gitelis or on my own," she explains. On these visits she always provides information on the patient's progress over the past 24 hours and answers questions. "Patients tend to ask the nurse more questions," Piasecki says, "probably because they think the doctor is on his way to operate and they shouldn't detain him."

One of her special responsibilities is pain management, a critical element of care especially for cancer patients. She often decides what medications are needed for pain and how they should be arranged with non-narcotic substances. Although Dr. Gitelis reviews and writes the prescriptions, Piasecki makes the decisions. "He respects my judgment," she says.

What could be a ticklish relationship—working with the nurses on the patient floor—is helped, Piasecki believes, by the Rush model for nursing, which sets a pattern for the "dovetailing" of responsibility for patient care.

"The joint practice nurse can be a threatening concept to the bedside nurse," Piasecki says. "Patients also can be confused as to who is really running the show." Piasecki is always very careful to explain to each patient that she is a consultant while they are in the hospital. "I don't do any hands-on nursing on the floor, but I do spend time with the unit nurses, explaining our long-range goals for each patient." And she believes the unit nurses, in turn, respect the fact that she has expertise in dealing with patients who have had the kinds of surgery the practice specializes in.

And what is the reaction of other physicians? Most of the orthopedic specialists, Piasecki points out, are in similar joint practices, so they are quite comfortable with the physician-nurse relationship. For the most part though, she says, other doctors don't understand what she does—until her work involves one of their patients. "When they discover the ways I help the patient, they are very grateful. In fact, some internists now call me first, rather than Dr. Gitelis, because they know I am more available since I don't go into the O.R. and am able to follow up on their requests."

In addition to patient responsibilities, she is also the clinical coordinator for the Medical Center's bone bank, for which Dr. Gitelis is the medical director. The bone bank supplies not only Dr. Gitelis' busy practice with bone for transplantation but procures, processes and stores bone that is made available to physicians and dentists throughout the country. As clinical coordinator, Piasecki knows where the bones come from and how they are screened, so she can address questions prospective transplant patients may have.

Piasecki's background includes special education in oncology and orthopedics. "At the time, I was simply interested in these fields, not looking toward a joint practice." But then, she says, Dr. Gitelis asked her to join him—and the resulting partnership has been not only professionally satisfying for the participants but a boon to their patients.

Special Services for Troubled Children

By Krys Kazieczko-Kuszak

Many parents seeking help for their children are already desperate when they first contact the Section of Child Psychiatry at Rush-Presbyterian-St. Luke's Medical Center.

"They often come with a file folder an inch thick with evaluations from previous places," says Elva Poznanski, M.D., the Woman's Board professor and director of child psychiatry.

At Rush, troubled children and their families are offered help through three different programs: a 15-bed inpatient psychiatric unit, the Rush Day School and outpatient services.

These programs stand out among those offered elsewhere for two main reasons: staff expertise in psychopharmacology, which is a relatively new area in child psychiatry; and a philosophy which insists on the family being actively involved in the treatment.

"Some people are surprised to learn that we use medications," Dr. Poznanski says. "They tell us that the kids appear so alert and really don't 'look medicated' at all. Well, what they need to understand is that psychiatrists use several different groups of medications, not just the very heavy tranquilizers that most people think of.

"We use medications, not as chemical restraints," Dr. Poznanski emphasizes, "but to help these children to settle down and to be able to learn, comprehend and function."

Whether children are admitted into the hospital, treated as outpatients or enrolled in the day school/ partial hospitalization program, parents or guardians are expected to be actively involved in the treatment program.

"We've been known to use everything under heaven and earth to get parents to work with their children in therapy," Dr. Poznanski says. "It's a requirement for admission to our programs."

Patients come from all over the city and its suburbs. They may have been referred by physicians, psychologists, therapists or school counselors. Many times parents themselves make the call.

"Typically, our patients have already had one or two or three rounds of treatment before they come here," Dr. Poznanski says.

That was the case with Joey.*

**Names in this story have been changed to protect patient and family identities.*

Elva Poznanski, M.D., stresses family involvement is a requirement for admission to the child psychiatry program.

"Typically, our patients have already had one or two or three rounds of treatment before they come here."

Elva Poznanski, M.D.

The Inpatient Unit

Joey wasn't a typical nine year old.

He'd sit cooped up in his room and come out only to eat or go to school. Music from his radio would blare, but Joey himself was an unusually quiet child, except for temper tantrums. Sudden outbursts were getting him into so much trouble at school that the principal was calling his parents at least once a week. He talked a lot about death and was terribly afraid of being kidnapped. That fear became such an obsession that he wanted his bedroom windows boarded up so that no one could break in and steal him away.

There were problems even before this.

Joey had a history of developmental difficulties—he needed occupational therapy to learn how to walk and didn't begin to talk until he was four years old. But Joey made enough progress to be enrolled in regular programs at his neighborhood public school. He was a quick learner and his grades were better than average. He did have problems, though, in relating to his classmates. He didn't make any friends at school and he also began to be more and more withdrawn at home. An unstable family life just added to the problems.

"Between my divorce and remarriage, I went through some pretty wild years," remembers his mother, Diana. "I had a lot of problems and needed to make many adjustments and the kids (Joey has a sister almost two years older) were with me through most of it," Diana explains.

Family life finally settled down, but Joey's problems didn't stop. He got into trouble stealing. If something bothered him he never talked about it at the time, but would later fly into a fit of sudden, violent rage, screaming uncontrollably.

"That's when the therapist Joey was seeing told me that he had too many problems for her to deal with," says Diana.

Psychiatric help was recommended.

"It wasn't easy for me to accept that at first and then it was very difficult to admit it to others," Joey's mother confesses.

"But as soon as I walked into the child psychiatry unit at Rush I liked what I saw. It didn't look like a hospital. And when I saw how wonderfully the staff related to the kids, I knew right away that I had made my choice."

Established three years ago, the child psychiatry inpatient unit at Presbyterian-St Luke's Hospital was carefully designed so that the boys and girls being cared for can, as much as possible, feel "at home." The children, who range from preschool age through 14, have regular bedrooms that they decorate with pictures, posters and drawings they've made, as well as favorite toys from home. There's also a game room, kitchen, laundry room, classrooms, an area for crafts and even a small gym.

The school program is accredited by the North Central Association of Colleges and Schools and

Linda Freeman, M.D., medical director of the inpatient unit, is shown in the gym, one of the unit's many special facilities.

teachers on staff are certified in learning disabilities and behavior disorders.

"Grades only tell a little bit of the story," Dr. Poznanski says. "Being able to look at what goes on in the classroom with the teachers we can see all the psychological aspects of the child trying to learn. We see how the child approaches learning and how he or she reacts in a classroom with other students. By seeing what the child avoids we might uncover some real learning problems because children, like adults, may try to 'save face' by refusing to do what, in fact, they can't do."

In recent years there has been a growing acceptance that children can have emotional disorders much like adults. They may suffer from depression, anxiety or eating disorders; show excessive aggression or other severe behavior or personality disorders. The problem may be a single one or a combination of two or more. All such cases and even the more acute—Tourette syndrome, organic brain damage with psychotic features, multiple personality—are treated at Rush.

"We probably get more children with depression or manic-depressive illness than other centers do," says Dr. Poznanski. "That might be because of our research (Dr. Poznanski and her colleagues are nationally recognized for their studies of depression in children), but it's probably just a part of the whole picture." Researchers estimate that almost half of American children who have some type of mental problem suffer from depression.

Before being admitted to the inpatient program at Rush, children and their families first meet with one of the board-certified child psychiatrists on staff who reviews the case to determine whether hospitalization is appropriate.

Children who enter the hospital go through an in-depth evaluation which takes about four weeks. It includes a comprehensive psychiatric assessment and a complete physical by Rush pediatricians. All services and resources of the Medical Center are available to assist in diagnosis and treatment so that pediatric specialists in such areas as neurology, behavioral pediatrics, psychology and endocrinology may also be consulted. A staff nurse trained in child psychiatry evaluates the child's behavior and assessments are also made by a social worker, occupational therapist and teacher.

When appropriate, children remain for treatment, and these staff members, together with the admitting child psychiatrist, become the patient's personal treatment team. If medical or neurological problems are involved—allergies, for example, or seizures, diabetes or asthma—these conditions may be monitored and treated right on the psychiatric unit, which is also specially equipped for just such cases. Most other psychiatric programs in a hospital setting would require that children with acute medical or neurological problems be transferred to a medical or neurological unit.

Members of the treatment team work closely with the child and family to tailor a treatment plan for their specific needs and also meet weekly in interdisciplinary conferences to monitor patient progress.

"Our goal is not to institutionalize these children and then send them to another institution," explains Linda Freeman, M.D., medical director of the inpatient unit. "Our program is designed to contact them and their families briefly, resolve the crisis, set them on a path of development and then discharge them to a less restrictive setting; in many cases that means going back home."

Since the inpatient unit first opened, about 100 children have gone through hospitalization. A typical hospital stay is about two to three months, Dr. Freeman says. "We've never had one of our children come back and be rehospitalized with us," she adds.

The program is successful, she says, because it strives to make necessary changes in the family environment to which the child will return. That depends on a willingness of parents, not only to cooperate, but to take an active part in the treatment.

"Studies have shown that the best sign that a child will do well in treatment is when a parent has difficulty leaving the child on the inpatient unit," Dr. Freeman says. "If a parent just wants to drop off the child and not be bothered, that could signal serious problems. We circumvent these problems by telling parents they must be actively involved."

Visiting is "prescribed." Sometimes the treatment plan calls for supervised visits, but in most cases visiting is open and parents are encouraged to participate in just about all the activities their children are involved in.

"Our staff is trained and willing and able to work with parents and their children on a day-to-day basis," Dr. Freeman says.

Other programs may limit parent involvement to structured family therapy sessions and rigid visiting hours but "we try to coordinate family therapy into milieu, which is what we call the day-to-day activities," Dr. Freeman says.

The daily schedule is much like a typical day for a child outside the hospital. There's breakfast in a "fam-

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INTO CLINICAL AND SCIENTIFIC PROGRESS IN MEDICINE
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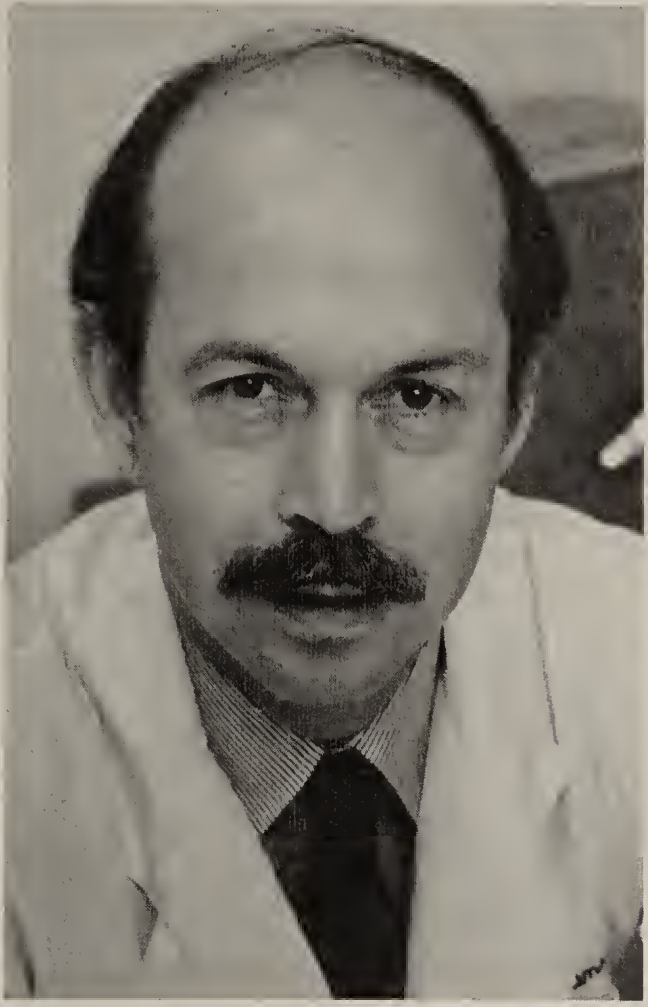
Transplanting the small intestine



James W. Williams, M.D.

The small intestine plays a major role in the breakdown of food from the stomach so that absorption of essential nutrients can take place.

Severe consequences can arise when this tubular organ does not function properly. One of the most common—a group of small intestine disorders called short bowel syndromes (SBS)—is caused by an inadequate absorptive surface.

James W. Williams, M.D., the Jack Fraser Smith professor of general surgery and director, Section of Transplantation, feels that many problems associated with SBS would be solved by successful intestinal transplantation.

These syndromes are becoming increasingly common because physicians are able to keep patients alive through the use of chronic parenteral nutrition (hyperalimentation), a process by which patients are fed through a tube inserted in a vein under the clavicle. "Although we are able to prolong lives with hyperalimentation," Dr. Williams says, "people with SBS still face a bleak and uncertain future." The major problem: once all potential veins for hyperalimentation access have been used, patients are unable to be fed and literally starve to death.

The effects of the debilitating short bowel syndromes can also lead to other severe complications such as liver and bone disease.

In spite of the advances in laboratory and clinical transplantation, the intestinal allograft has remained resistant to long-term success. By 1984, there were seven reported attempts at small intestine transplant in humans, but these patients all died soon after transplant.

Dr. Williams believes the most likely explanation for the difficulty in establishing long-term survival lies with the lymph tissue. "The great volume of lymphoid tissue transferred with the intestine either induced a degree of sensitization and rejection response that could not be predictably controlled or produced the lethal graft-versus-host disease," he says.

For the past four years, Dr. Williams and his colleagues have been evaluating graft irradiation as a means of modifying transplanted lymphoid tissue using a canine animal model.

Lymphoid tissue, located in the mesentery and inside the intestine, is part of the body's immune system and protects the body from outside toxins and bacteria. Lymphoid cells transferred with the intestine during transplantation are highly sensitive cells and react to foreign proteins. Therefore, they will try to reject the recipient, causing graft-versus-host disease.

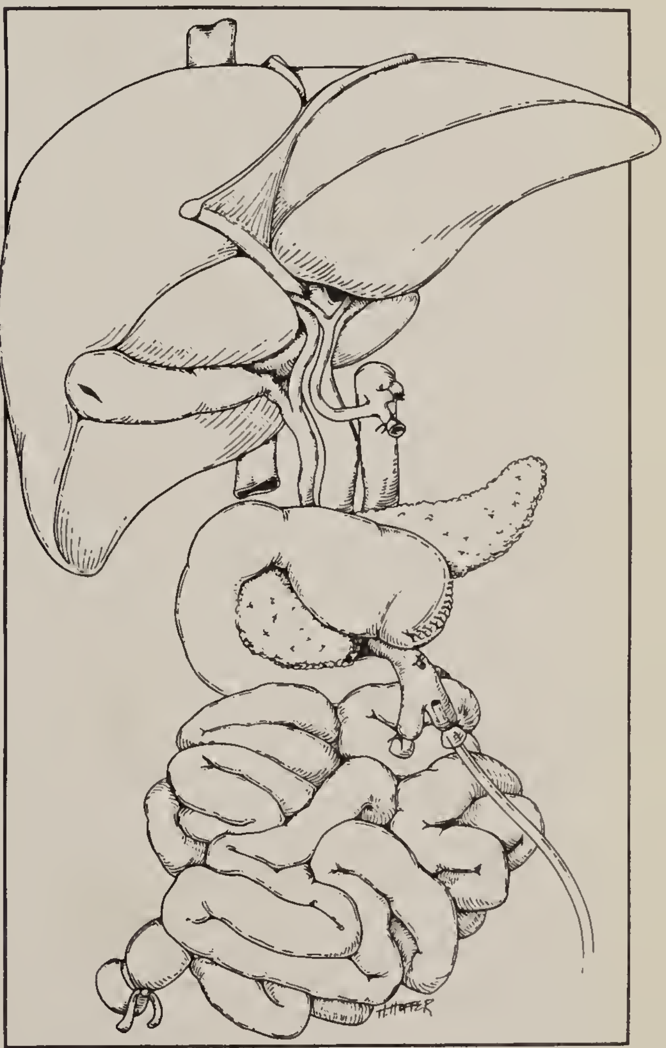
But these cells are also the most sensitive to radiation, so most lymph cells can be killed with low doses of radiation, thereby reducing the chance of rejection, yet saving the much-needed mucosal cells which also line the intestinal wall.

Although radiation has long been used for relatively selective destruction of lymphoid tissue, the dose, which optimally inactivates or destroys graft lymphocytes yet spared the intestinal wall, had not been defined under the cold ischemic conditions required in organ preservation and transplantation.

Through extensive work with canine animal models, Dr. Williams developed a technique by which an adequate dose of radiation can be administered which appears to kill the lymph cells yet maintains the integrity of the small intestine.

But the radiation of the intestine itself appears to produce considerable immunosuppression. This, coupled with the high dose of the anti-rejection drug cyclosporine, caused excessive immunosuppression and death from infection. By decreasing the dose of cyclosporine, Dr. Williams was able to control rejection and diminish infection-related death.

In a related project using rat animal models, Dr. Williams is studying the types



This is the ***en bloc*** *multi-organ graft. Included in the composite illustration are a portion of the stomach, small bowel, liver and pancreas. The tied-off end of the small bowel (lower left corner) will become the site of an ostomy. This end is later hooked up to the colon. The tube (lower right corner) is used to flush blood from the graft and administer preservation fluid during the transplant. The tube is later removed.*

of lymphocytes regenerated following irradiation and subsequent transplantation. "We hope they are recipient lymphocytes, not donor lymphocytes," Dr. Williams says.

But, solving the problems surrounding small intestine transplant may not be the total solution for small infants who lack a small intestine and must be fed through hyperalimentation.

While hyperalimentation provides these infants with all the essential nutrients to sustain life, it also causes rapid liver deterioration. The cause of this degeneration is unknown, but the result is a fatal liver disease. Infants with this condition usually don't live past 18 months.

The only hope at this time is a highly experimental multi-organ transplant: a donor small intestine to allow nutrients to be absorbed by the body and a donor liver to replace the rapidly failing liver.

Dr. Williams and his colleagues are currently working to develop a successful model for this multi-organ transplant.

Says Dr. Williams: "With the resolution of each problem surrounding small intestine transplantation, we come closer to offering this type of therapy to the thousands of people affected by debilitating and life-limiting short bowel syndrome."

Mary-Ann Redeker

Collaborating with Dr. Williams on this work are: Preston Foster, M.D., general surgery; Howard Sankary, M.D., general surgery; and Inchul Lee, M.D., pathology.

Studying aging

Aging—irreversible and, to date, not very well understood.

"It's invalid to look at aging unless you have a viable system to study," says Jerome R. Kuszak, Ph.D., senior scientist, Department of Pathology, Rush-Presbyterian-St. Luke's Medical Center. Dr. Kuszak has spent the past 12 years, first at Wayne State University, then at Rush, developing methods to make the eye lens a reliable model to study aging at the cellular level.

Until now, researchers studying aging have most commonly used cells in culture. These *in vitro* studies were limited in scope because their results by definition had to be qualified. What was needed was a human or comparable *in situ* animal model which presented the whole aging picture.

The lens of the eye maintains every fiber cell formed in fixed locations throughout a lifetime—from the first trimester *in utero* to death. It also grows continuously throughout life so within one lens there is a cell that has just been formed and a cell that is the age of the person. "Thus, the lens provides a unique model to study structure-function relationships of cells throughout the aging process," says Dr. Kuszak.

"Basically, we're ultrastructural cell biologists working on aging," he explains. "But through our work with the lens we've made some interesting discoveries about cataracts."

Senile cataracts are a consequence of aging—everyone will form them if they live long enough. They are the number one cause of blindness in the world, the number three cause in the United States.

The focus of the work at Rush is on the cause of senile cataracts. This work has led to some remarkable findings about the structure of the lens.

Using a multi-step dissection process, Dr. Kuszak and his colleagues were able to access accurately and reliably every cell in the lens so that comparisons could be made between cells of different ages using stereoscopic scanning and transmission electron microscopy (SEM and TEM) and the freeze-etch technique.

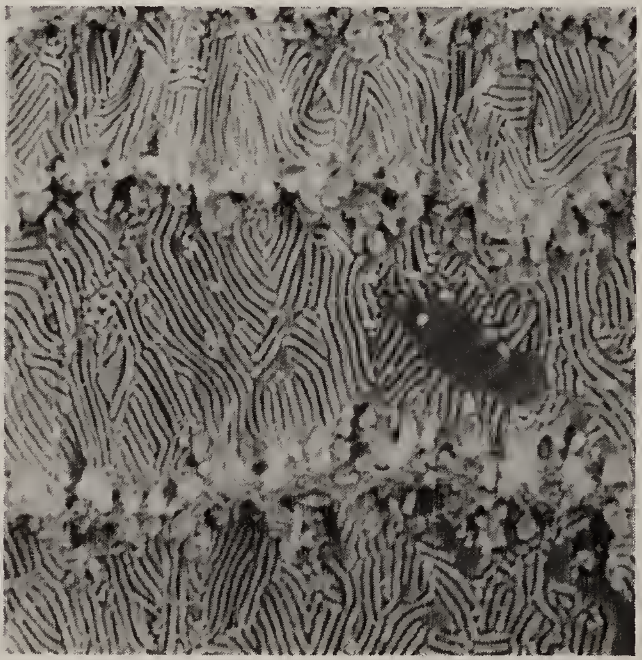
Ultrastructurally, all the fiber cells are essentially crescent-shaped and are hexagonal in cross-section profile. The youngest cells have a very smooth membrane. In stark contrast, the oldest cells have furrowed membranes with innumerable elongate microvillae (fingerlike projections).

These findings are consistent with other aging studies which have shown increased remodeling of cell membrane is a consequence of aging. Researchers had proved this in culture systems but this was the first time it was shown *in situ*.

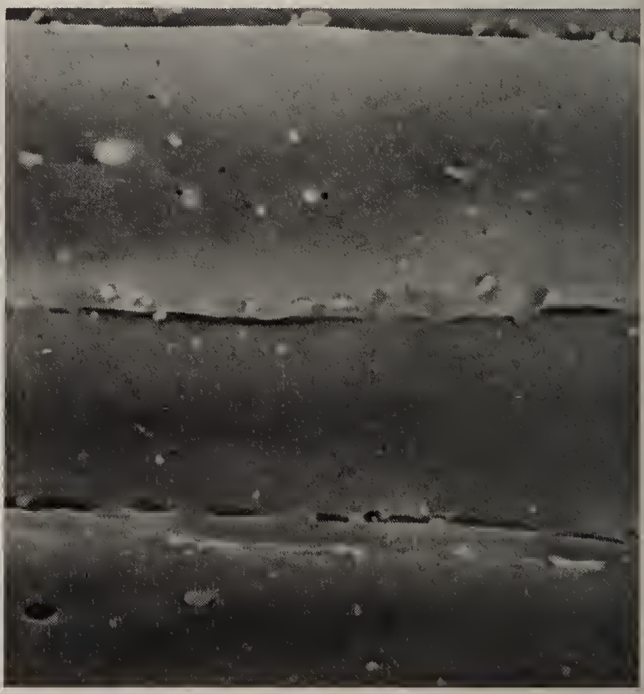
In addition, this is the first demonstration of an ordered pattern and the formation of microvillae as a function of age.

It was presumed that lens transparency was due to the parallel arrangement of the flat surfaces of fiber cells. The discovery of the dense cover of microvillae on the furrowed membrane would be contrary to this theory. Closer examination showed that order is not only necessary, it is of a magnitude beyond what had been realized.

"What researchers didn't realize, because they had never been able to access all the cells, was how accurate they really were," says Dr. Kuszak. "The cells were ordered and symmetric beyond everyone's wildest imagination.



The most senescent cell (from a 70-year-old senescent human cataractous lens)



The youngest cell (from the same cataractous lens)

Jerome R. Kuszak, Ph.D.

"The older cells in senile cataracts continue to be transparent," Dr. Kuszak says. "Problems arise in the younger cells which become incapable of remodeling to create the necessary interlocking of the microvillae." *(see photographs at left)*

Researchers don't know why these younger cells are incapable of remodeling and are searching for answers in the biochemical processes of lens cells.

If the search for a cause is taken to its logical extension, they hope to find ways which may delay the development of senile cataract or aging effects in other tissues.

Says Dr. Kuszak: "With our *in situ* system, we have established structure/function relationship for the lens and have set ourselves up to look at change in these relationships as a function of aging and pathological conditions of the lens, such as cataracts."

Mary-Ann Redeker

Funding for this research comes from the National Eye Institute and the Otho S.A. Sprague Memorial Institute.

Collaborating with Dr. Kuszak on the research are: Ronald Weinstein, M.D., the Harriet Blair Borland professor of pathology; Harry Maisel, M.B., Ch.B., Wayne State University; George Pappas, Ph.D., University of Illinois; Candace Ennesser, M.Sc., and Kathleen Chapman, research associates, Department of Pathology. More than 12 Rush Medical College students have assisted Dr. Kuszak in his research.

Understanding Alzheimer's caregivers

Alzheimer's disease is a progressive, irreversible neurological disorder that causes confusion, dementia, memory loss and eventual death.

Caring for a person with Alzheimer's disease has been referred to by some as "the 36-hour day." To date, the majority of research funding has gone to finding the cause and cure for this devastating disease. But little is known about the people who care for its victims. What medical and emotional concerns do these caregivers have? What types of support do they need?

At Rush-Presbyterian-St. Luke's Medical Center, Carol Farran, D.N.Sc., R.N., assistant professor, psychiatric nursing, is the principal investigator of a longitudinal study examining the characteristics of caregivers who participate in different education support programs and the effects of these programs on caregiving skills.

The focus of the first-year pilot study was to compare three different caregiving groups to better predict what types of people would be more likely to use particular types of services.

The three caregiver groups were:

- those in an eight-week, structured group with a strong educational focus led by mental health professionals (Dr. Farran and colleagues developed this program).
- those in an unstructured, ongoing Alzheimer's Disease and Related Disorders Association (ADRDA) group led by caregivers.
- those in a non-treatment community contrast group.

Participants were recruited from the Rush Alzheimer's Disease Center, Johnston R. Bowman Health Center for the Elderly, home health care agencies and ads in the media.

All caregivers were initially interviewed in their homes. Members of the education group completed a second questionnaire immediately after the eight-week intervention program, and participants of all three groups were interviewed ten months following their initial interview.

Of the 44 caregivers in the study, most were spouses, the remainder children and other family members or friends.

The education group's care-receivers were not impaired as long or as severely as those cared for by members of the other two groups. Onset of the disease occurred less than four years ago; physical impairment was slight to moderate, while cognitive impairment was moderate to severe.

Preliminary group characteristics emerged after the initial interview. The education group tended to use the fewest number of agencies and professionals, and reported higher levels of distress over their family members' memory loss, even though their relatives had fewer memory problems. The ADRDA group turned more frequently to agency and professional assistance.

On the whole, caregivers basically cared for their relatives out of love and mutuality. The exception was daughters who said that they were primary caregivers because of the absence of others to care for the family member and lack of money.

Although the activities of all caregivers were equally restricted, the adjustment to changes in activities was more difficult for caregiving wives and daughters than for husbands and sons.

"We found that caregiver husbands brought previous job attitudes and skills to the caregiving process and tended to use a problem-solving approach," Dr. Farran says. "Wife caregivers, on the other hand, expressed more emotions and grief, which may account for the adjustment difficulties."

But, males in the education group felt significantly less prepared to meet the physical personal care needs of their care-receivers.

Uncertainty of the future ranked high as a concern among all caregivers. Those expressed included: an inability to take a break or vacation; the unpredictability of their relatives' moods or state of mind; and concern about what would happen if they could no longer care for their relatives.

In the eight-week evaluation of the education group, there was a significant increase in positive coping and problem-solving behaviors; a slight increase in caregiving satisfaction, and no increase in care-receiving negative behaviors.

However, distress over their family member's memory problems increased. "One possible explanation for this is that the group experience provided caregivers with a better understanding of the disease process and what the future probably held for them and their impaired relatives. Another possible explanation is that caregivers in the education support group may have given more socially sanctioned responses during the initial interview, but were more candid after the eight weeks because the appropriateness of so-called negative feelings had been validated through group discussions," Dr. Farran explains.

Caregivers in all the groups reported that they obtained their caregiving knowledge primarily through experience, supplemented by reading. Professionals provided little to some information, while family and friends of the community group provided very little.

Ninety-three percent of participants in the education group felt that their objectives were met considerably to extremely well. Eighty percent indicated that the group assisted them in solving particular caregiving problems such as managing physical and behavioral problems. The most beneficial aspect of the group was being able to share concerns openly and feel supported by other group participants and by leaders.

Carol J. Farran, D.N.Sc., R.N.

Based on these results, Dr. Farran feels that an intervention program is needed during early to middle phases of caregiving.

"We'd like to follow these caregivers over an extended period of time," she says. Since the completion of the pilot study, a few of those receiving care were placed in nursing homes or have died. Researchers want to find out what happens to caregivers when they place family members in a nursing home, how their lives change after the placement and, following the death of the relative, how they put their lives back together.

Debra Williams

Funding for this study comes from the Alzheimer's Disease and Related Disorders Association, the National Institute of Mental Health and the College of Nursing, Rush University.

Co-investigator: Eleanora Keane-Hagerty, M.A., research associate, psychiatric nursing, The University of Chicago.

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Writers: Mary-Ann Redeker
Debra Williams

Editor: Mary-Ann Redeker

> *"Studies have shown that the best sign that a child will do well in treatment is when a parent has difficulty leaving the child on the inpatient unit."*
>
> **Linda Freeman, M.D.**

ily" setting with the staff, getting ready for school, classes, gym, and after-school activities including arts and crafts, games and play time. Field trips are usually scheduled on Tuesday afternoons and a liberal pass system allows children to go off the unit for occasions like a birthday celebration at home or a special shopping trip downtown.

Occupational therapy is part of the everyday activity, especially for preschoolers or children with developmental problems.

"If a child does not have the coordination to be involved in games, it's very difficult to form relationships with peers, since play is an important way of interacting," explains Barbara Rodriguez, OTR/L. "We spend a lot of time working on the sub-skills of play."

Keeping the schedule to what a child would do in a typical day helps identify the problems a child may face in everyday life and also helps to make for a smooth transition back to the community.

"Sometimes during playtime parents say 'that's just how he behaves at home'," Rodriguez adds. "This helps us identify the kinds of frustrations the child faces in everyday life and what the parents identify as problems."

Nurses and social workers on staff work very closely with parents and children to develop the skills they need. For parents it could mean learning how to discipline or how to play and have fun with their children; for the youngsters, it could mean learning how to deal with anger or talk out problems.

"Some of the closest relationships people have are within their families and they can be some of the most intense, both positive and negative," says Kate Mayton, M.S., R.N., nursing coordinator for the section of child psychiatry.

"But we've seen some wonderful progress in the families that come to us," adds Mayton, who is a clinical specialist in child and adolescent psychiatric and mental health nursing. "Working with children is encouraging because if we catch things early enough, we could help prevent lasting damage or help to develop some good adaptation. Even children with some of the most difficult conditions—those who have retardation or developmental delays or psychotic features—show a remarkable ability to adapt, compensate for their deficits and try with everything they have to make it."

Discharge planning by a social worker helps the family and child make a smooth transition back home and into the services they need, which might include therapy, special education or medical follow-up. There is also a joint meeting with teachers from the school the child will be attending, even if he will be going back to the same school.

"Emphasis on family involvement in the treatment takes a lot of energy, but the results are worth it," according to Nancy Donovan, M.S.W.

"I might need to put in a lot of time to engage the family in the process so that everyone begins working together, but then things click. All the problems are not necessarily cured, but enough has changed through the hospitalization that the family has a sense of direction. That's a reward point—when I know they can leave here and continue their work."

It's been a little more than a year now since Joey was discharged from the hospital. He talks about his stay on the unit in casual conversation and refers to it as a happy time.

"I have no trouble talking about it because I think it's the best thing we ever did," says his mother, Diana.

Joey's diagnosis was depression. His hospital stay lasted three months and "didn't just help Joey, it

Artwork by former patient, "Joey," shows his concept of the gym, one of his favorite places for recreation during his inpatient stay.

helped our whole family," according to Diana.

"During visits we did normal, everyday things together, like playing games or going over homework. When problems came up the staff was very supportive and I learned from watching them deal with Joey. Then we focused on these problems in family therapy. We got a lot of things talked out and worked out in those sessions."

At the same time, Joey's teacher on the unit made sure he continued his studies, so there was multiplication to study and two-digit subtraction with regrouping in math, plus spelling and reading and all the other lessons in the educational plan developed specially for him.

He went bowling on a field trip, made a spice rack and wooden notepad holder in crafts and liked to play basketball in the gym. Free time in the evenings often included a game of Chutes and Ladders or working on a jigsaw puzzle. In all, Joey made 11 different puzzles, each featuring a favorite cartoon character such as He-Man or Snoopy, and all proudly displayed on his bedroom floor.

And just like at home, Joey also had responsibilities—keeping his room neat, for example, and getting ready for school on time. A system of points kept track of everything he should do each day so that he knew what was expected of him. If he did everything well, he'd get three points, if not so well, one or two. A point total within a certain range earned a treat. The system worked so well, Diana says, that she continued it at home for a year and then adapted it to a simpler check system which she still uses today.

After two months Joey showed marked improvement and was allowed to go home on weekends. "Medications that fit with his temperament kept him going and kept him calm," Diana remembers. "His points were getting better every day and he was learning how to control his temper. When something bothered him, he'd tell me, 'okay, I know it's time to do steps one, two, three'; I was amazed to hear him say that."

But perhaps the most significant change, Diana notes, is that Joey would finally say what was on his mind. "Before I'd go home at night we'd sit on his bed and really talk. It was something we could never do before. They (the staff) opened up tremendous doors for us."

Joey was discharged from the hospital in time to celebrate Christmas at home that year and now attends his neighborhood public school. He still sees a therapist and continues medication, but as Diana points out, "he's 100 percent better today."

A Middle Step

Although many patients, like Joey, return home following hospitalization, some troubled youngsters require a "middle step" between hospitalization and home. The Rush Day School fills that need.

Children aged 5 to 14 who are enrolled in this program live at home and come to school at the Medical Center Monday through Friday year-round. Most have both emotional and learning problems. For many, medical disorders further complicate their conditions.

The private therapeutic school is equipped to accommodate 21 students, and includes three levels: primary, for 5 to 7 year olds; junior, 8 to 10; and senior, 11 to 14. Teachers with master's degrees, who are certified specialists in learning and behavior disorders, tailor individual lesson plans according to each student's particular needs and level of functioning.

Accredited by the North Central Association of Colleges and Schools, the Rush Day School program received high marks for the way its staff works together. Psychiatrists, teachers, nurses, social workers, and recreational and occupational therapists provide an interdisciplinary treatment approach. The overall student-staff ratio is three to one.

Home base is the classroom, but students go to the craft room for art projects and also receive adaptive physical education. Health classes taught by nurses twice a week focus on safety, the senses, body functions and other health-related topics.

"Most of our children have had a lot of school failure and they're afraid to fail again, so our program is designed to give them support while learning demands are made on them," explains Gracia Guise, M.S., executive director of the school. "Lessons are prepared in such a way that the child can do the work and feel some sense of success."

The outpatient services program provides the medical, psychiatric, nursing and therapy services these children need.

Their problems cover a wide range. Some youngsters are hyperactive and not able to sit still very long; some provoke other kids with their behavior; some are autistic and withdrawn into their own world, or severely depressed or suffering from a psychosis.

With a physician and nurses on staff, even very medically ill

> *"Before I'd go home at night we'd sit on his bed and really talk. It was something we could never do before. They (the staff) opened up tremendous doors for us."*
>
> **Diana, Joey's mother**

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children—those with seizures, severe asthma or diabetes, for example—can be admitted to the program. One troubled child with cancer attended the Day School while undergoing chemotherapy at the Medical Center.

"Many children in our program might ordinarily be cared for in a hospital or residential setting," notes outpatient services director Karen Pierce, M.D., a board-certified child psychiatrist. "But because we have a good staff, good family treatment and good family support, these kids are really able to be maintained on an outside basis."

Children are usually enrolled in the Day School for a year or two, as was one graduate whose parents brought him to Rush after trying several other therapeutic schools without success. His diagnosis was pervasive development disorder—impairment in three areas: social ability, communication skills and learning skills. "When he came to us he was nearly 14 years old and he did not know how to cross a street or count money," Dr. Pierce notes. "In our program, he learned how to do those things and more. For example, he now has friends and calls them regularly on the telephone. While he still needs the support of a restricted setting, he is doing wonderfully."

Careful discharge planning assures that as students leave the Rush program they are already linked with whatever special services they require. Teachers and social workers meet with representatives from the school district the child will be attending.

Just as in the other child psychiatry programs at Rush, parental involvement is a must. "We work closely with parents," Guise says. "We see them in therapy individually, as couples and as families because there have to be some changes in the family and the way the parents deal with the child if the child is going to improve overall.

"During parent-child sessions," Guise explains, "the child will almost always demonstrate the problem behavior and the parent very often does not try to deal with it. In that case the family therapist steps in and manages the child as a role model." Parent education meetings are also held to offer support and provide a forum to discuss issues such as building positive relationships, limit-setting with your child and making time for yourself.

In group therapy two days a week youngsters learn how to get along with their peers. They also meet with a therapist individually as well as the sessions together with their parents.

The Day School is in operation year-round, including the summer months.

"When I visit the classrooms, I see that the students are interested in what they're learning and seem to be having fun," says Dr. Pierce. "Kids tell me that they love to go to school here." ❂

Implantable Pump Brings Relief from Spasticity

By Carolyn Reed

You know what a charlie horse feels like. Agony. It's the middle of the night, and you've stretched in your sleep: a sudden cramp in your calf wrenches you awake. Desperately you massage the muscle or force yourself to walk, to stretch it out of spasm.

Now imagine being confined to a wheelchair, your lifeless legs wrenched by similar spasms on and off, all day as you try to go about your business, all night as you try to get comfortable in bed. Your legs go stiff and rigid. They feel heavy as lead, you can't lift them or pry them apart. And though you supposedly have no feeling in them, they may ache from the intense contractions. They are out of your control.

That is spasticity.

Spasticity is a complication of neurologic injury. People who've suffered an injury to their spinal cord and people who have neuromuscular diseases like multiple sclerosis or cerebral palsy may experience bouts of spasticity. It may occur only occasionally or it may occur frequently. But when it is frequent, it is often severe, and life becomes unbearable.

Oral medications for spasticity do exist: baclofen (Lioresal) is used most commonly, diazepam (Valium) may be used as well. But because of the marvelous and perplexing "blood-brain barrier" baclofen in oral doses doesn't get very far in the nervous system, while diazepam causes drowsiness and confusion.

There are surgical ways to deal with spasticity as well, which is why such patients will seek out a neurosurgeon. Richard Penn, M.D., is professor and senior attending surgeon in the Department of Neurological Surgery at RPSLMC, and over the years has seen many patients with severe spasticity.

"What neurosurgeons have been doing for spasticity is injure the nerves to interrupt the spasm: they do a myelotomy. Or they will cut the nerve root, a rhizotomy. But these aren't minor operations. They're very drastic measures. They do permanent damage. I felt there had to be a better way."

And he has found one.

He uses an implantable, programmable drug pump to deliver minute amounts of antispasm medication (baclofen) directly into the cerebrospinal fluid. The pump is manufactured by Medtronics, Inc. It's about the size of a hockey puck, made of the space-age metal, titanium. It weighs about 10 ounces, has an 18 cc drug reservoir, and is controlled by a microprocessor which can be programmed to deliver medication at varying rates. Dr. Penn was the first and, until now, the only U.S. physician authorized to implant this pump to treat spasticity.

Dr. Christine Branson of Evanston was one of his first "pump patients." Dr. Branson is paralyzed from the waist down as a result of a horseback riding accident in April 1985.

By August of that year the then-36-year-old internist was sufficiently recovered and accomplished at getting around in a wheelchair that she was discharged from the Rehabilitation Institute of Chicago.

"The spasticity came on quite suddenly. Within a period of two weeks I completely lost my ability to maneuver in and out of my wheelchair. Just moving in bed could bring on excruciating spasms. The spasms were so bad that I couldn't lift my foot off the footrest (of the chair). I had to use so much energy to control the spasticity I had no energy left for anything else."

> *"There's no way I could've hoped to become independent again without the pump. I couldn't wash myself, dress myself, or use the bathroom. I don't know what would've happened to me if this (accident) had happened to me 20 years ago."*
>
> **Dr. Christine Branson**

Spinal cord patient Dr. Christine Branson (left) shows how relaxed her legs are as a result of pump implant by crossing one for neuroclinical nurse specialist Suzanne Savoy, M.N., R.N. Savoy, trained as a critical care nurse, follows all pump patients closely, is available around-the-clock to answer questions and sees them as outpatients regularly for pump check-ups and refills.

Her anti-spasm medication dosages were quickly upped to 80 mg/day baclofen, as well as 80 mg/day diazepam and 400 mg/day dantrium.

"There's no way I could've hoped to become independent again without the pump. I couldn't wash myself, dress myself or use the bathroom. I don't know what would've happened to me if this (accident) had happened to me 20 years ago."

Christine consulted Dr. Penn, and in December 1985, became one of the first people in the U.S. to have the drug pump implanted to control her spasticity. Her *daily* medication dosage is now 0.6 mg baclofen.

Drug pumps are not new, but the programmable pump Dr. Penn uses was only developed in the early 1980s, and until recently, had only been used clinically to deliver pain medications and chemotherapy regimens. It remains an investigational (i.e., experimental) device.

But the pump offers a straightforward solution to the problem of penetrating the blood-brain barrier. Biomedical engineer Jeffrey Kroin, Ph.D., is Dr. Penn's co-investigator. He notes, "We have really two circulatory systems in our bodies, our blood system and our cerebrospinal fluid (CSF) system, which bathes the spinal cord and our brain. The blood passes through the central nervous system, but because of the way its capillaries are designed, very little of what's in the blood ever reaches our nerve cells. This protects the central nervous system from a host of bacteria, viruses, drugs and other threats, but makes it difficult to treat diseases of the brain and spinal cord."

By inserting the pump's catheter directly into the subarachnoid space of the spinal column, in the lumbar region, medication is delivered directly into the cerebrospinal fluid. The blood-brain barrier is bypassed.

Dr. Penn began his work with the programmable pumps in 1982. That year he became the first U.S. surgeon to implant a programmable pump in a cancer patient, to manage intractable pain.

At the same time, with Dr. Kroin, he began investigating the possibility of delivering other medications to the CSF. Dr. Kroin, who is associate professor of neurosurgery and physiology, used rabbits to test the efficacy of intrathecal baclofen infusion on normal animal reflexes.

"Our questions were 'can we get the drug directly to where we want it to work?' and 'can we make it affect only a certain part of the nervous system?'" He found that drug infusion through a catheter placed in the spinal fluid bathing the lumbar area of the rabbits' spinal cord altered the rabbits' reflexes in the hind legs but not the fore legs. It was the effect they were hoping for. "After all, we wanted to relieve spasticity in our patients' legs, but not compromise the use of their arms and upper body."

Next they tried a small but direct injection of baclofen into the CSF of human patients with severe spasticity. It worked, providing the same relaxation effect for 6-8 hours. "But you can't chronically treat spasticity that way," he notes. "So the pump supplies the 'chronic injections.' "

The pump itself is placed just under the skin, in a pouch created within the abdominal fatty tissue. Then the pump's catheter is tunneled under the skin around to the patient's back and inserted into the lumbar subarachnoid space of the spinal column. The procedure takes about an hour. Subsequent refills are done every few weeks through the skin, by inserting a needle into the pump's raised rubber filling port.

Drs. Penn and Kroin are concluding a second study of 20 patients using the pump. Participants have either a spinal cord injury or multiple sclerosis. In this study they've been joined by physiatrist Barbara Parke, M.D., who sees the patients prior to the implant and follows their course for a year after, to evaluate the pump's effect on their disability.

Dr. Parke is assistant professor of physical medicine and rehabilitation, and clinical director of rehabilitation medicine at RPSLMC. She defines spasticity as a kind of *hypertonicity*, an extreme increase in the normal state of muscle tone.

"Spasticity comes from two sources, the brain or the spinal cord. The exact details aren't known and there are various theories as to what triggers it, but with a spinal cord injury in particular, what's left are reflexes without any inhibition.

"These patients come into our study because they've tried everything and they can't control their spasm."

She notes that while the vast majority of spinal cord patients have some degree of spasm, not all are disabled by it. Forty-six-year-old Jim McCormick of South Holland is a good example. Injured in a motorcycle accident in 1975, he is quadriplegic, with only limited use of his upper arms. Yet he didn't begin to suffer severe spasticity until nearly ten years after his accident, following a series of abdominal operations. He was taking up to 120 mg diazepam and 80-100 mg of baclofen daily just prior to his pump implant in August 1987.

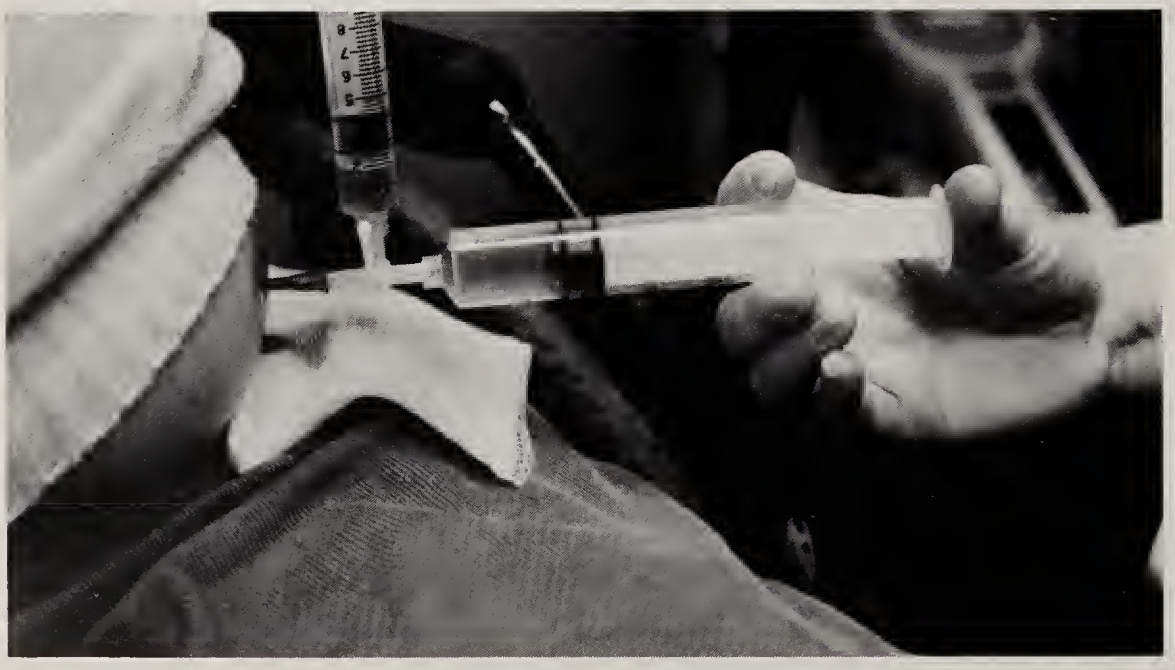
"I didn't have too many side effects, but I was needing more and more of the medications. And the spasms disrupted my sleep. My legs would just bounce out of bed."

He says the pump has both benefits and drawbacks for him: "I'm almost too relaxed in the chair now, since it was my spasms that kept me upright. On the other hand, it's a lot easier to get dressed since my mother can now move my legs."

Dr. Parke sees prospective pump patients on their first day in the hospital when she does her initial evaluation. "I always ask the patients, 'What do you hope to get from this?' and they always answer the same: 'More independence, less spasticity, increased comfort,' and variations on that. And the improvement we see subsequently is unbelievable.

"Some of our MS patients are free of their Foley catheters, and several can get around with crutches or a walker; the pump has meant that some can return to work."

Donna Jettner of Charlotte, Michigan, has experienced a remarkable improvement in mobility since her pump implant in January 1987. The 40-year-old secretary and mother of two was severely spastic from her multiple sclerosis; her right leg



Periodic refills are done through the skin. A raised, rubber portal on the pump makes it relatively easy to locate the refill site. The needle is then inserted through the portal, whatever medication remaining inside the pump is removed (top cylinder) and new medication is inserted.

> *"The possibilities are endless now that we have a way to bypass the blood-brain barrier."*
>
> **Richard Penn, M.D.**

would draw up in spasm making it almost impossible to walk. She was nearly housebound for a year. So she scheduled herself for nerve-cutting surgery. Then she learned of Dr. Penn's work and had the pump implanted instead. Now she can walk (with assistance), drive, and has returned to work. "I have my life back again."

For all the remarkable results, however, pump implantation remains an investigational procedure, closely monitored by the FDA and out of reach to many patients for now. Intrathecal baclofen is an experimental drug, not approved for this use in this country. Dr. Penn hopes that will soon change. A ten-center trial of intrathecal baclofen administration for spinal cord and MS patients has just begun in this country under his direction. And a multi-center study is already underway in Europe, also under Dr. Penn's direction.

Recently the FDA granted Dr. Penn approval to investigate the efficacy of intrathecal baclofen administration in patients with spasm from cerebral palsy, dystonia, and head injuries.

But perhaps most significantly, this early work with spastic patients has opened the door for myriad applications of implantable drug pumps in neurologic disorders. Because pump technology offers a better way to deliver a variety of drugs directly into the central nervous system, at doses far below those used orally or intravenously, with greater efficacy and few if any side effects, it's now being tested for treating brain tumors, ALS, Parkinson's, and Alzheimer's disease.

In cooperation with researchers at Dartmouth-Hitchcock Medical Center in New Hampshire, Dr. Penn is using an implantable pump in a small number of Alzheimer's patients. With these patients the medication is delivered intraventricularly: the catheter is tunneled up to the head and inserted directly into one of the brain's ventricles. There it can bathe the brain in a particular medication. So far, bethanocol has been tested, with limited success. Dr. Penn also predicts the implantable drug pump may have applicability in treating Parkinson's.

"We are studying the CSF of our Parkinson's patients who've undergone the adrenal implants (see p.), in an effort to better understand what substance changes in their brains after the implant. Then perhaps we could manufacture that 'something' and pump it in directly."

Another Alzheimer's study will begin soon, using a compound similar to somatostatin (a brain chemical believed deficient in Alzheimer's patients). It's thought that this drug, pumped directly into the brain's ventricles might improve memory and cognitive function in these patients.

"The possibilities are endless now that we have a way to bypass the blood-brain barrier. It's an exciting time for neurology and neurosurgery."

Jeffrey Kroin, Ph.D., (left) and Richard Penn, M.D., are shown with multiple sclerosis patient Donna Jettner, who can now walk with crutches following her pump implant.

A Day in the Life of the Alzheimer's Disease Day Care Center

by Debra Williams

A nostalgia calendar hangs on the wall. An entry reads: "Ozzie Nelson —born March 20." Most of the people who come here, along with their families, grew up with Ozzie, his wife, Harriet and the rest of the Nelson family. Now ask these people who the Nelsons are and they are puzzled. They don't know.

Jack (not his real name), once the vice president of a prominent bank, could speak five languages, including Russian. Ask him his name. He can't remember.

The day is beginning at the Alzheimer's Disease day care center on Chicago's northwest side. The room is filling up with senior citizens from a variety of backgrounds —housewives, laborers, accountants, salesmen—who share the same problem. Most not only can't remember their names, they can't remember why they are here or where they live. They are victims of Alzheimer's disease—a progressive, irreversible neurological disorder which causes confusion, gradual to severe memory loss, mental deterioration, and, eventually, death.

The staff greets each arrival, setting the tone for the day's activities. "Gene, you're the last one to arrive. Here let me take off your coat. How are you today?"

The day care center is a collaborative effort between Rush-Presbyterian-St. Luke's Medical Center, the Chicago Area Chapter of the Alzheimer's Disease and Related Disorders Association (ADRDA) and the Westside Veterans Administration Medical Center. One of only a handful of such centers in the United States, it was organized in 1987 as an alternative to nursing home placement. It is staffed by five health care professionals from the Medical Center and two from the Westside V. A. as well as two trainees from the City of Chicago's Title 5 Program which places citizens over 55 years of age in job training programs for two years. Members of the ADRDA serve on the steering council of the day care center which provides the facility with advice and financial support. Currently the staff serves 32 clients. There is a waiting list for applicants because of the center's increasing popularity.

Before being accepted at the day care center, the prospective carereceiver and his/her family are interviewed to determine if the client is eligible for this service. The day care staff then put in many long hours of phone screenings and interviews discussing the client's medical history, behavior at home, family interaction and the history of the dementia's progression. The center takes clients with moderate to severe dementia, unless their behavior indicates severe aggression or they will require more than one staff member to care for them during the day.

"Okay let's see what's in the paper today. The Winter Olympics are finally over. Does anyone know what events were held? (There are one or two responses.) "Good! Has any one here ever been sledding or ice skating?"

One of the attractions of the day care center is that clients are not just dropped off to sit for eight hours, —with a break for lunch—then sent back home again. Throughout the day, their minds are challenged and stimulated. Each morning a staff member reads current events from the newspaper, and gently probes the clients with questions to stimulate memory.

"We know that there is no cure for Alzheimer's disease," says Sara

“We’ve found that people often retain music when other memories have disappeared.”

Melanie Chavin, R.M.T.-B.C.

Sandy Thompson, recreation technician, coaxes a smile from one of the clients.

Van Winkle, R.N., the day care director under the Rush Alzheimer’s Disease Center, “but inactivity can help slow down thought and we believe that keeping mentally and physically stimulated is better than being inactive. It may even help.”

The daily newspaper has been read. It is close to 11:00 a.m. Melanie Chavin, R.M.T.-B.C., a registered music therapist and the center’s activity director, pulls out her guitar and plucks out a few notes. It’s now time for music therapy. “Does anyone know this song?.” she asks, as she strums out “I Left My Heart in San Francisco.” Surprisingly, many clients begin to sing the song, word-for-word. After leading the group in other songs about cities and places, Chavin asks, “What places can you remember visiting? (“Morocco,” one says. “Ireland,” says another.) “Great! Can anyone else think of a place that they’ve been to?...”

Music therapy is a popular feature of the program. It is used to bring the group together, to create moods, to energize clients when they are tired, to stimulate long-term memory and to help clients reminisce.

“We’ve found that people often retain music when other memories have disappeared,” says Chavin. She recalls when one man, on hearing familiar music, wanted to dance with her. “I told him I didn’t know the dance steps, he would have to teach me. And he did!

“Music is an important part of our society.” Chavin explains. “Growing up you listen to it, you dance to it and it’s part of many special events like weddings and graduation. I guess people don’t forget it easily.”

Music therapy is over, for now, and it’s time for lunch. The men and women are settled into chairs and hot lunches and milk are passed out. “How’s your lunch, Sally? Good, I’m glad you’re enjoying it.” Sally is hugged.

Throughout the day, there are many, many hugs and words of affection and encouragement. To work with these clients requires energy, sincerity, patience and a deep commitment.

“Working with our clients can sometimes be frustrating but it also can be a lot of fun,” says Lisa Hill, a recreation technician at the center. “For me, it’s like caring for a lot of grandparents. It’s a great feeling.”

A short time later, Hill invites one of the clients to sit next to her. The client is hugged. Hands are intertwined. They sit together holding hands for some time.

After lunch, the men and women are divided. The men play ring toss and the women have their hair combed, their faces made up and their fingernails polished. One of the men successfully tosses a horseshoe over the middle post, scoring the hiqhest possible point.

“Did everyone see that? Tom, do you see what you did? That was great!” Tom’s face lights up with pride.

Everyday clients are encouraged to do simple gross motor activities like ring toss, bowling and basketball. These and other planned activities not only provide exercises they provide accomplishment and help boost self-esteem.

An example is the weekly cooking class. “If we make a casserole,” Van Winkle explains, “one person opens cans, others chop vegetables or grate cheese. These are simple tasks for us, but it takes them much more time to complete them. But they are busy and working toward a goal.”

Often families are surprised at what their relatives accomplish at the center. “She makes salad!” one astonished husband asked a staff member. "She can't do that at home." But the center staff often has more time than families to devote to letting clients do things for themselves.

"We find out what it is our clients like to do, and we work around that," says Chavin.

During the spring and summer, groups are taken for walks. This time is used not only for enjoying a little fresh air but, as Van Winkle explains, for "reality orientation. We talk about flowers blooming, nature, the environment—anything that is stimulating. We are always watchful for situations that best provide a physical or mental benefit to the clients."

The staff also works closely with their clients' families. Once a month, family members meet at the center to discuss problems, share suggestions, even exchange phone numbers for future conversations and comfort. Each meeting has a focus and sometimes special guests are invited to talk about specific topics requested by family members. Families are also encouraged to join the support groups of the ADRDA.

The response from families for the center's work is positive...and grateful.

"I don't know what I would have done if it were not for the day care center and its staff," says the wife of a client. "The day care center gives me some relief during the day and I don't have to worry about unconcerned strangers caring for him."

It was because she had no one she could trust to watch her husband during the day that she was forced to retire early.

"I couldn't even go grocery shopping," she says. "I'd take my husband with me, strap him in his seat belt, lock him in the car, rush into the store like a madwoman and grab whatever I could off the shelves and dash back out to the car before he was able to undo his seat belt."

Not only has the center given her time to take care of errands, but she believes the day care center has been good for her husband.

"He was so lethargic before," she says. "But now, he comes home and he picks up objects and examines them. He seems interested in the things around him. The things the staff have done for him represent true dedication."

Currently the staff, in collaboration with the Rush Alzheimer's Disease Center, is conducting a comparative study of people who are receiving this type of respite care and those who are receiving no special care. Some of the questions the study hopes to answer are: Whether respite care attenuates the psychological distress experienced by caregivers; whether or not day care can delay long-term institutional care; the impact day care has on the physical and financial status of the caregiver; whether or not day care can slow the decline in cognitive functioning, and whether or not day care can slow the decline in activities of daily living.

Carol Farran, D.N.Sc., R.N., instructor, psychiatric nursing, Rush University College of Nursing, is studying ways to help families cope better with the disease (See *Insights* insert in this issue). Other researchers at the Rush Alzheimer's Disease Center (see sidebar) continue to search for a cure for the disease. Until then the center's staff will do what they can.

At the day care center, the day is ending and it is time for the clients to return home. Staff members

Music therapy is directed by Melanie Chavin, R.M.T.-B.C., activities director and music therapist at the center.

> *"Working with our clients can sometimes be frustrating but it also can be a lot of fun. For me, it's like caring for a lot of grandparents. It's a great feeling."*
>
> **Lisa Hill, recreation technician**

Reading the newspaper is an important part of the daily activities. Dale Johnson, an intern from the National College of Education, leads this session with the news.

leave to start and warm up the center's two buses. Most of the clients will be taken home by the day care center staff or will be picked up by family members.

"Okay Joe, it's time to go home. I'll get your coat and help you put it on, okay?" Joe smiles.

"Sometimes this job can be tiring and frustrating," says Hill. "But when you see a smile, when you see the difference it makes in these people's lives and in their families, it makes it all worthwhile."

It is now after 5:00 p.m. and all the clients are gone. The staff trades anecdotes as they prepare and plan for the next day. Another day filled with both frustration and small triumphs has passed,—everyone looks forward to tomorrow.

The Rush Alzheimer's Disease Center

The Rush Alzheimer's Disease Center is one of the first programs in Illinois to offer comprehensive diagnostic evaluation, neuropsychological testing and extensive family support services. Designated by the state as the Regional Center for northern Illinois, the program makes it possible for patients and families to obtain all needed services related to the disease at one location.

The Center is co-directed by James Schoenberger, M.D., the Charles J. and Margaret Roberts professor and chairman of preventive medicine at Rush-Presbyterian-St. Luke's Medical Center, and Jacob Fox, M.D., a recognized authority on Alzheimer's disease and associate professor of neurological sciences at Rush University.

At the Center, correct diagnosis is the first step. Testing may include magnetic resonance imaging, a highly sophisticated procedure that detects the loss of brain cells, an electroencephalogram, which measures brain waves, comprehensive blood tests and evaluations of memory, speech and cognitive abilities.

After the evaluation is complete, family members meet with a neurologist, psychologist and social worker to discuss the patient's condition, what they can expect in the future and what resources and support services are available to them in their own communities and at the Medical Center.

Programs of care are tailor-made for each patient and family and assistance is offered in making appropriate arrangements for in-home nursing, day care (see accompanying article) or nursing home placements as needed. The Center also trains volunteers for home hospice care of Alzheimer's disease patients in the terminal stages of the illness.

Research is also an important facet of the Center. In one study, information from each patient on genetic, demographic and environmental influences that could be risk factors in the development of Alzheimer's disease is entered into a computerized registry for future study. Patients may have the option of participating in controlled clinical trials of new drug treatments.

The Center saw its first patients in October of 1985 and has so far evaluated some 600. *K.O.*

Research Planned for Gallstone Lithotripter

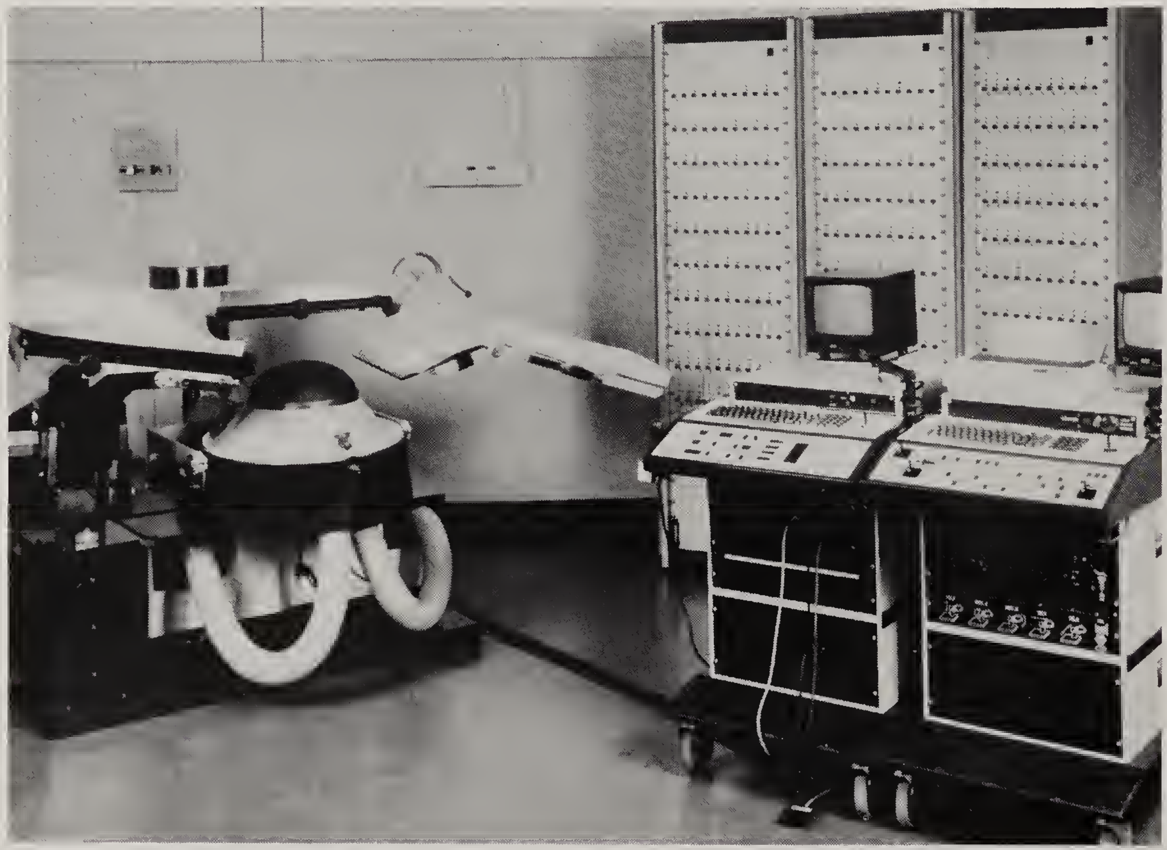
A new device that destroys gallstones without surgery on an outpatient basis, without hospitalization, and requiring little or no anesthesia, has been delivered to a group of practitioners based at Rush North Shore Medical Center, a corporate affiliate of Rush-Presbyterian-St.Luke's Medical Center.

Investigators from Rush Medical College will conduct research and assay results of the experimental equipment as part of a study approved by the Food and Drug Administration (FDA). The research team is headed by Seymour Sabesin, M.D., the Josephine Dyrenforth Professor of Gastroenterology and director of the Section of Digestive Diseases.

Called the EDAP LT.01, the machine is a new generation lithotripter manufactured in France that already has been used successfully on kidney stones and gallstones in Europe and Asia. It is located in Rush North Shore's professional building; the facility is known as the North Shore Biliary and Renal Lithotripsy Center.

Leonard Berlin, M.D., chairman of the Department of Radiology at Rush North Shore Medical Center and a member of the group that purchased the equipment, noted that there are an estimated 475,000 gallstone operations in America each year, approximately one-fifth of which could be replaced by gallstone lithotripsy. The EDAP LT.01 procedure, which can be done in less than an hour, does not require bodily immersion as do first generation lithotripters. Last year EDAP obtained an Investigational Device exemption (IDE) from the FDA to begin treatment of kidney stone patients in the U.S. Results from clinical investigations led EDAP, whose American offices are in Westford, Massachusetts, to file for premarket approval from the FDA. EDAP also has recently applied for an IDE to begin gallstone lithotripsy testing at selected sites in the United States. Rush-Presbyterian-St.Luke's will lead clinical investigations for gallstone lithotripsy in the Midwest, studying patients of the North Shore Biliary and Renal Lithotripsy Center.

The new machine is already functioning and in vitro demonstrations have been completed in which gallstones suspended in fluid have been disintegrated by shock waves from the EDAP machine. Procedures on actual patients will begin in the summer.



The EDAP LT.01 lithotripter could reduce gallstone operations by approximately one-fifth.

New Procedure Aids Breast Biopsies

Painless, less disfiguring breast biopsies are now possible, thanks to a new technique at the Medical Center. This technique, called stereotoxic needle biopsy, was developed in Sweden and brought to this country by Kambiz Dowlat, M.D. Dr. Dowlat, who recently joined the medical staff as associate professor, general surgery, tested the technique at The University of Chicago. The Medical Center is the third institution in the country to offer this alternative to surgical breast biopsy.

Says Dr. Dowlat: "This outpatient procedure allows us to biopsy small non-palpable breast lumps, discovered by mammography, without causing scarring or disfigurement to the breast."

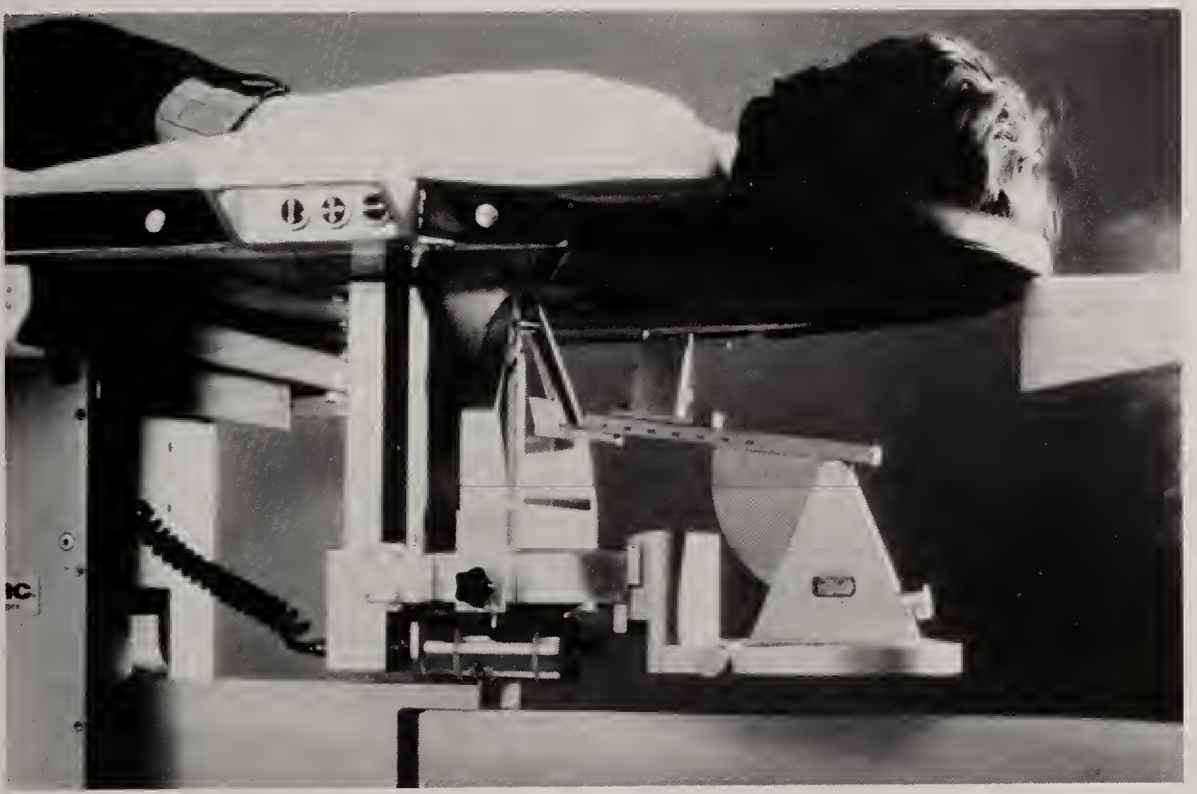
Local anesthesia is used with minimal discomfort to the woman. The biopsy is performed, using a device which consists of a modified mammographic machine and a needle module attached to an examining table. With the help of a small computer, the non-palpable breast lump is first re-visualized and then precisely (within 1 mm) localized for fine needle (22 gauge) sampling. The procedure takes 30 to 40 minutes to perform, and costs half the amount of a surgical biopsy.

"The greatest advantage of this technique is that it discriminates between malignant and noncancerous shadows discovered by mammography in the breasts of otherwise healthy women," Dr. Dowlat says. While modern mammography is very sensitive in detecting early breast cancer with low radiation to the breast, it cannot discriminate these shadows with a high degree of accuracy. Therefore, radiologists are currently recommending that women with suspicious shadows in the breast undergo biopsy. Eighty percent of all suspicious breast masses detected by mammography are not cancerous. With the needle biopsy procedure, many women are spared disfiguring surgery.

"Based on my two-and-a-half-years' experience in 300 cases, supported by a larger experience reported from Germany and Sweden, stereotaxic needle localization and cytologic diagnosis have an accuracy of 95 percent," he says.

The device also enables Dr. Dowlat to pinpoint the exact location of the suspicious lump in cases when open biopsy is requested. "If the woman wishes to return to her own physician for surgery, the device allows us to insert a very fine wire in the exact area of the mass," he says. "Again, this helps lessen the distortion of the breast tissue in future evaluation by mammography."

Dr. Dowlat received his medical degree from the University of London. His research interests include diagnosis of metastatic breast lesions using radio labelled monoclonal antibodies and other projects related to prevention and treatment of breast cancer. M-A.R.



For the biopsy procedure, the patient is positioned on an examining table to which a modified mammographic machine and a needle module are attached.

Parkinson's Surgery Testing Underway

"These patients are better; we don't know if this improvement will persist or if it relates to anything more than a placebo effect. We are cautiously optimistic," says Christopher G. Goetz, M.D., associate professor, neurological sciences and pharmacology, referring to an experimental transplant surgery for Parkinson's disease patients under study by researchers at the Medical Center for the past year.

Parkinson's disease is a chronic nervous disease characterized by tremor, slowness, rigidity and a shuffling gait. Its cause is linked to the failure and death of certain dopamine-generating nerve cells in the brain. Today it affects as many as one million people in the United States and one to two percent of people over age 60.

The surgery, first reported in April 1987 by Mexican surgeon, Ignacio Madrazo, M.D., of the Hospital de Especialidades Centro Medico, Mexico City, is being tested at the Medical Center by researchers from the neurology and neurosurgery departments.

Seven patients with Parkinson's disease have had the surgery at the Medical Center. The first was done in June of 1987. The patients are under 60 years of age (mean age 47); all are afflicted severely with the disease and are either severely disabled, or unable to move independently for part of the day. All had been coming to the Medical Center as outpatients for treatment of Parkinson's disease for about a year.

Neurosurgeon Richard Penn, M.D., and general surgeon, Thomas Witt, M.D., simultaneously perform the transplant surgery which takes about five to seven hours to complete. In preparation for the Medical Center's study, Dr. Penn went to Mexico City to learn Dr. Madrazo's surgical procedure for the transplant.

The experimental surgery is called autologous adrenal medulla transplant. It is really two operations. While the neurosurgeon is doing the craniotomy, or opening of the right side of the head, the general surgeon opens the stomach to remove the right adrenal gland, located on the kidney. Bits of gland tissue are dissected under a special microscope and procured. Meanwhile, the neurosurgeon goes into the brain via the ventricular system and removes some ventricular fluid. This is examined for the presence of dopamine and other chemicals.

"A small sample of the caudate nucleus is then removed," explains Dr. Goetz, "and in that place the adrenal tissue is inserted. A ventricular catheter is also inserted into the right lateral ventricle and connected to a reservoir. By this means we can measure the presence of brain chemicals post-operatively."

In the days after the surgery, while patients are still in the hospital, Rush researchers have not regularly observed the two-day "honeymoon" from Parkinson's symptoms and medications as Dr. Madrazo reported with two of his patients. That is, most of the transplant patients continue to have symptoms and to require medication. "By six months they do show a modest improvement in their response to one medication, Sinemet," Caroline M. Tanner, M.D., assistant professor, neurological sciences, says. "Fluctuations appear less frequent and we see that patients' 'on' time (good performance of daily living functions) is longer than their 'off' time when symptoms are so severe that they can't get out of bed or a chair unassisted."

The ventricular fluid is studied once a week for the first two weeks after the surgery, then at three months and every six months thereafter. Fluid is checked for dopamine, norepinephrine and other chemicals. The research team see patients for neurological evaluations weekly for two months and then monthly for two years.

"Their 'on' time is definitely longer," says Dr. Goetz. "This is probably the greatest benefit of the transplant surgery. However, patients could be better because of some as yet undetected trophic factor which is stimulating nerve growth. We don't know yet.

"We're waiting until we have one year's data to decide whether or not more of these transplants will be done at the Medical Center," says Dr. Goetz.

For now the Rush Parkinson's disease researchers are sharing information about their transplant protocol with other centers doing the surgery and at meetings sponsored by the United Parkinson's Foundation. C.E.

Rush Performs Second Multi-Organ Transplant

The second multi-organ transplant to be performed at Rush-Presbyterian-St. Luke's Medical Center was done in February on a seven-month-old baby boy. The child was suffering from short gut syndrome. In the ten-and-one-half-hour operation, James W. Williams, M.D., transplanted a new liver, small bowel, pancreas and a portion of the stomach. As this issue of the *Magazine* went to press, the young patient, who had survived for three and a half months, succumbed to multiple organ system failure.

"This is a very experimental procedure," says Dr. Williams, the Jack Fraser Smith professor of surgery and director of the Section Transplantation. "But the alternative for children suffering from a malabsorption disorder is early death."

Only four such transplants have been performed in the United States, and only one other patient, a three and a half year old girl at Children's Hospital, Pittsburgh, survived more than a few days. The first Rush operation, was performed in 1986 on a 22-month-old boy who also had short gut syndrome.

"We learned a lot from our first multi-organ transplant. Our first patient lived three days, and our second patient benefited from what we learned as a result," says Dr. Williams.

For the past five years, Dr. Williams has been studying intestinal transplantation in animals, as a

Carmela and Terrence Barrett, of suburban Chicago, proudly show off Meghan Marie, Ryan Matthew and Kathleen Anne, the first triplets born in the Medical Center's In Vitro Fertilization Program. The program, which opened in 1983, has produced a total of 20 babies. It is headed by W. Paul Dmowski, M.D., Ph.D., director of Reproductive Endocrinology and Infertility in the Department of Obstetrics and Gynecology.

means of treating various fatal malabsorption syndromes in humans. Intestinal transplantation success has been hampered historically by the donor bowel's immune system. Unlike other donor organs, the small bowel has a very high concentration of immune cells in its mucosal lining. Dr. Williams used preoperative radiation of the bowel to suppress its immune response, in combination with aggressive postoperative immunosuppression and infection control.

"Conceptually, multi-organ transplantation should work," Dr. Williams says. "But there are still some technical problems that can only be worked out in human trials."

Rush Joins Poison Consortium

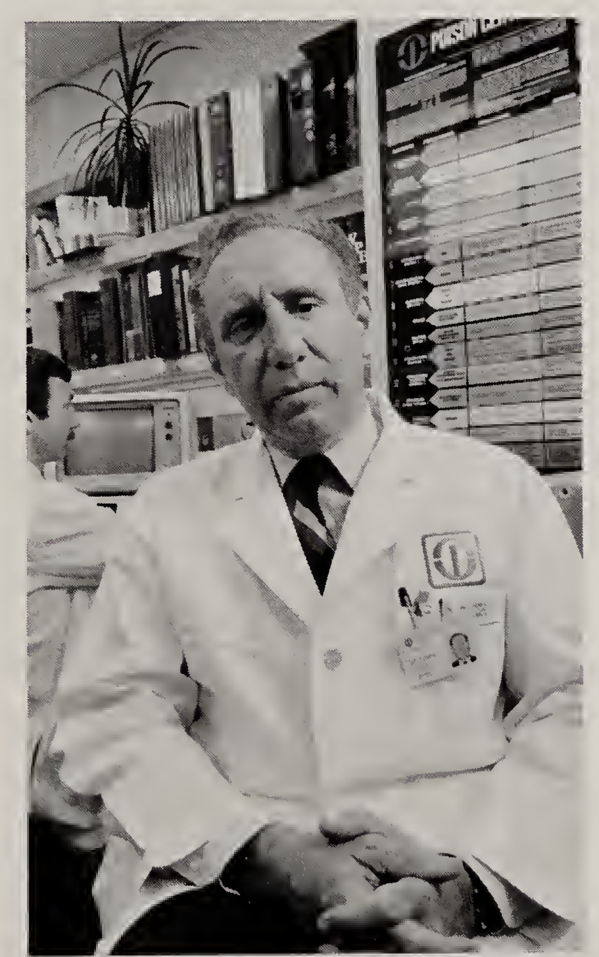
Acute poisonings are the fifth leading cause of accidental death in the United States. "But, because of a shortage in manpower, fragmentation of services across institutions and a deteriorating financial climate, it is clear that no single institution is capable of providing patients at risk of poisoning with the full spectrum of poison information as well as clinical and education services," explains Paul Pierpaoli, M.S., R.Ph., director of the Medical Center's Department of Pharmacy and professor of pharmacology.

The Medical Center, University of Illinois and Cook County Hospital think they have found the answer to this problem in Toxicon, a consortium combining the toxicology resources and capabilities of the three institutions. Funding for Toxicon comes from a Chicago Community Trust grant of $722,000.

The Departments of Pharmacy and Pharmacology at the Medical Center bring to this group years of experience in research and consumer issues through their Poison Control Center, the first in the country, having been established in the early '50s. Through its College of Pharmacy, the U. of I. operates an extensive drug information service for physicians and health care institutions and supports a very active epidemiology program in its School of Public Health. Cook County Hospital is strong in industrial and environmental toxicology and the kinds of problems that result from chronic or acute exposure in the workplace or environment.

Consumer and health care professional education, the establishment of a full range of clinical toxicological services and toxicological research are three broad-based goals of the consortium.

More specifically, Toxicon has singled out children six years of age and younger, drug abusers, drug-attempted suicides and the industrial and environmental sector for in-depth education and a full range of services. "For instance, children six years old represent 64 percent of the acute poisonings in the United States," Pierpaoli notes, "and the Illinois Environmental Protection Agency handles 400 potentially serious industrial or environmental toxicological incidents every year."


Paul Pierpaoli, M.S., R.Ph., shown in the Medical Center's Poison Control Center.

Through its six objectives, Toxicon hopes not only to reach its target groups but also expand and fine tune its delivery of information on identification and treatment of poisons. Of equal concern is antidote availability. In a recent mock disaster drill involving an industrial chemical accident in the Chicago area, only ten percent of the required specific antidote was available. "Given our highly industrialized area and population density, lack of an antidote could create a major public health problem," Pierpaoli says. "Toxicon will also assist in depoting selected poison antidotes."

In addition, Toxicon will provide active epidemiological surveillance, using state-of-the-art computer systems and networking, and assist in providing an early warning system for situations such as recent salmonella outbreaks due to dairy products and cyanide tamperings of consumer products. This system allows epidemiologists to identify index cases and immediately alert the public and governmental agencies.

There are some five million known chemical entities in existence. The scientific community has toxicological information on approximately 50,000 of them. Much is known about pharmaceuticals and drug and food additives but they represent about 10,000 to 15,000 substances at best.

"The development of new compounds continues and far exceeds our capacity to keep up with knowing about the toxicology of these substances and how to manage acute and chronic exposure to them," Pierpaoli says. The research component of Toxicon will respond to this problem with avenues for sharing information in the scientific community. Predisposition to toxicity, currently being studied in children with chronic lead poisoning, and the testing of more effective antidotes are other research interests.

"We have many challenges ahead of us," Pierpaoli concedes. "Through institutional cooperative efforts like Toxicon, we have hopefully found a response." M-A.R.

Center Studies Teen Suicides

When most people think of research, their immediate frame of reference is the study of diseases of the body. The objective: learn more about the disease to improve treatment, perhaps find a cure, and even prevent the disease. But how does a research scientist investigate the *mind* for clues about future self-destruction?

The Center for Suicide Research and Prevention was established in 1985 to illuminate the nature of suicide through research which will lead to new and better methods of assessment, treatment and prevention.

A major research effort begun in 1987 is the exploration of teen suicide. Suicide among teenagers 15 to 19 years of age is the second leading cause of death in the United States. The goal of the innovative study is to reconstruct the suicidal teen's state of mind prior to the event.

David C. Clark, Ph.D., assistant professor of psychiatry and psychology, and director of the Center for Suicide Research and Prevention, is leading a multidisciplinary team in a three-year study which will reveal and document the psychological and emotional factors present in the teen's mind which predisposed him to complete the act. (Four times as many girls *attempt* suicide and four times as many boys *die by suicide,* according to center pyschologists.) Further, the researchers hope to pinpoint how the "completed suicides" differ from attempters.

"There is little information about this group—those who commit suicide," says Dr. Clark. "Most studies focus on the ones who attempt suicide, but do not die. We're looking at all teens in a three-county area (Cook, Du Page and Lake) because we want to shed light on the reasons why these young people are killing themselves in record numbers." Dr. Clark points out that in Illinois there are 60 to 70 suicides annually involving young people 15-19 years old.

Dr. Clark and the faculty of the Suicide Center have devised a scientific method for "psychological autopsies" which consists of eight to 10-hour interviews with parents, siblings, grandparents, best friends and others close to the victims.

Hartmut Mokros, Ph.D., director of child and adolescent research at the Suicide Center, defines a psychological autopsy as "a reconstruction of the psychological profile of the suicidal person at some period prior to his death."

Once the county coroner has determined that a suicide death has occurred, the family is asked if they wish to participate in the psychological autopsy study. Of the 42 determined suicides in 1987, 39 of the families agreed to be interviewed. It appears that almost all the families have a need to talk about the suicidal event.

The researchers plan to complete 120 family interviews during the study. The diagnostic interview contains 200 questions which assess the family's psychopathology, and indicate any relationship between affective disorders, namely depression, and alcoholism and substance abuse, both high-risk factors for suicide. Dr. Clark reports that the interviewers are finding two-parent families: most of these parents have no history of psychiatric treatment. Besides the interviews, records and reports from teachers and counselors, the family physician, the coroner and police, plus any messages left by the deceased teen are examined.

An interesting finding at this point is that the teenager's friends have a "sense" that something is awry prior to the actual suicide, And preliminary analysis of data also shows that most of the suicidal young people had talked about taking their own lives, or they had told someone, maybe a best friend, that they were going to do away with themselves.

"We want to find out if the young person had any long-standing personality problem, such as moodiness, low self-esteem or narcissism. There could be mention of one of these problems, for example, in the family doctor's medical history of the teenager," Dr. Mokros explains. "Also, we want to know if the victim had a prior suicide gesture, such as an overdose of pills. With this knowledge, we can work with the family and siblings and friends to find ways to prevent future suicides."

The Rush researchers conducting interviews do not counsel the families, but they refer parents, siblings and others to support groups, such as LOSS—Loving Outreach to Survivors of Suicide. LOSS group meetings offer a time to share ideas, feelings and hope.

The teen suicide research project includes two comparison groups: the "normal" group—teenagers from the same neighborhood as the suicidal youth who are interviewed to determine a level of psychological illness in the community—and parents of a second group of teenagers who died as passengers in a car accident.

Dr. Clark and the researchers are planning to apply the psychological autopsy method to another series of teenagers who die suddenly and violently—those who die in car accidents. It will be valuable, he says, to compare this group with the teenagers who die by suicide. "We want to put our project information into the hands of schools, clergy, physicians and others," Dr. Clark says, "so that they can know the factors in the minds of teens who take their lives. We need to intercept them. We need to do it soon." C.E.

RushRounds

Commencement 1988

Rush University conferred 354 degrees at its 16th annual Commencement, June 11, at Medinah Temple. An honorary doctor of humane letters degree was awarded to commencement speaker, Samuel O. Thier, M.D., president of the Institute of Medicine of the National Academy of Sciences.

"As professionals you're responsible for maintaining and passing on knowledge and serving others," Dr. Thier told the graduates. "In all of what we do, we must consider not just biology, but public health implications: epidemiology, nutrition, social sciences....We must consider prevention, and not simply reversal of disease, as our primary strategy."

Harold Byron Smith, Jr., Board of Trustees chairman, and Leo M. Henikoff, M.D., Medical Center President, presented degrees to 121 doctors of medicine, eight doctors of nursing science, and 11 doctors of philosophy. Another 115 graduates received master of science degrees: 68 in nursing, 2 in audiology, 9 in clinical nutrition, 16 in health systems management, 15 in occupational therapy and one in anatomy.

Ninety-two students received bachelor of science degrees in nursing, eight in medical technology.

Three Trustee medals honored individuals whose outstanding contributions advanced the ideals of the Medical Center and provided exemplary standards for generations to come. Recipients were:

Evan M. Barton, M.D., professor of internal medicine and a medical staff member for 52 years; Mrs. George S. Chappell, Jr., a Life Trustee and past president of the Woman's Board; and the late Ormand C. Julian, M.D., Ph.D., pioneer cardiovascular surgeon and a past chairman of the Department of Cardiovascular Surgery. Dr. Julian's award was accepted by his widow, Rosemary Julian. K.O.

College of Nursing undergraduate Melissa Mruskovich.

Rush-Presbyterian-St. Luke's at the Atrium

"It makes no sense to spend $2 million on the very latest equipment, technology and quality facilities set into 20,000 square feet of space and then treat the patient like he or she is waiting in line at a discount store," said Cheryl Erdmann, director of the Medical Center's recently opened medical offices/information center at the Northwestern Atrium Center.

"As a result, we've hired an especially qualified support staff who are concerned about the patient's work schedule and time constraints; as well as how he or she feels."

Opening week June 6 saw the Atrium's services already in demand with patient visits ranging from sore throats and ear aches to cardiac stress evaluations. Hundreds of people have browsed through the information center where free health and wellness bro-

Assisting Dr. Henikoff in officially opening the Atrium offices are (l) Trustee Bide L. Thomas and Atrium director Cheryl Erdmann.

chures are on display.

The Atrium facility includes 31 private patient examination rooms and 17 physician/client consultation rooms on the fourth floor, plus a Concourse level information center. Both are open from 7 a.m. to 6 p.m.

Said Medical Center President Leo M. Henikoff, M.D.: "The Atrium represents further regionalization by the Medical Center, also reflected by the establishment of our satellite offices at One Financial Place and River City, as well as a half dozen dispersed occupational health centers for the metropolitan work force."

Services offered at the Atrium medical offices include internal medicine, obstetrics, gynecology, plastic and reconstructive surgery, medical oncology and gastroenterology. Among the specialty centers are a Prostate Evaluation Center, for diagnosing prostatic diseases (including cancer) by ultrasonic imaging, and the Pap Smear Center, which emphasizes prevention of cervical cancer.

An examination program for corporate executives, and a young adult medicine program combining family practice, pediatrics and internal medicine are also available.

M-A.R.

New Trustees Join Rush Board

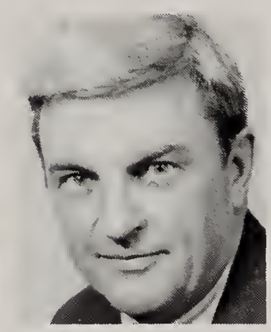
Five new trustees were elected to the Medical Center's board. They are:

Earl Abramson, chairman, president and director of Rapid Mounting and Finishing Company. A graduate of the University of Michigan, he has served on the boards of Rush North Shore Health Services and the Bureau of Jewish Employment Problems.

Hall Adams, Jr., chairman and chief executive officer of Leo Burnett USA. A graduate of Williams College, Mr. Adams has headed the United States operations of Leo Burnett since 1982. He is the creator of a number of distinguished advertising campaigns, including the United Airlines' Friendly Skies and the Harris Bank Lion.

William C. Glenn, president of Olsson Roofing Company, Inc., of Aurora, Illinois. Mr. Glenn, a graduate of Dartmouth College, holds a master's in business administration from Amos Tuck School. He is a director of the Merchants National Bank of Aurora, Merchants Bancorp, the Aurora Economic Development Commission and the Aurora Foundation.

Earl Abramson


Hall Adams, Jr.

William C. Glenn

Mrs. John H. McDermott

Andrew Thomson, M.D.

Mrs. John H. McDermott who will assume the presidency of the Medical Center's Woman's Board in fall. A graduate of Washington State University, she is a director of the Visiting Nurses Association of Chicago, the Ravinia Festival Women's Board, the Unibanc Trust Company of Chicago and the Women's Board of The University of Chicago.

Andrew Thomson, M.D., senior attending physician in the Department of Internal Medicine. A medical staff member since 1963, Dr. Thomson earned his medical degree from Indiana University. He chairs the Board of Overseers of Dartmouth Medical School, and is a past trustee of the Chicago Medical Society and a member of the Institute of Medicine.

Rush Adds Endowed Chairs

Three new endowed professorships have been established at the Medical Center and two Medical Center physicians and two scientists have been named to endowed chairs by the Medical Center's Board of Trustees.

A generous bequest from the estate of Charles J. and Margaret Roberts, founders of the Roberts and Hart Packing Company in Chicago, provided for the establishment of the following chairs:

The George W. Stuppy, M.D., Professorship in Arthritis

The James B. Herrick, M.D., Professorship in Heart Research

The Charles J. and Margaret Roberts Professorship in Preventive Medicine

The philanthropy of the Roberts grew out of a relationship with their close friend and physician, the late George W. Stuppy, M.D., the first president of the merged Presbyterian-St. Luke's medical staff.

The Medical Center's new named professors are:

- Ruggero G. Fariello, M.D., the Jean Schweppe Armour Professor of Neurology: Dr. Fariello, who is chairman of the Department of Neurology, is a native of Turin, Italy. He came to the Medical Center from Thomas Jefferson University in Philadelphia, where he was professor of neurology and pharmacology, vice chairman of the department of neurology and director of clinical neurophysiology. He received his M.D. degree from the University of Turin. Dr. Fariello, an authority on epilepsy, is certified by American boards in electroencephalography, neurology and psychiatry, and is well known for his research and writings.

- Elva Poznanski, M.D, the Woman's Board Professor of Child Psychiatry: Dr. Poznanski, director of the Section of Child Psychiatry, is an internationally recognized authority on childhood depression. She developed the Children's Depression Rating Scale, a test now routinely used to assess depression severity in children 12 years and younger. Dr. Poznanski is board certified in psychiatry and child psychiatry, and is the author of numerous articles on childhood depression. She currently serves as chairperson of several national subspecialty boards in child psychiatry.
- Thomas P. Andriacchi, Ph.D., the Claude N. Lambert, M.D.—Helen S. Thomson Professor of Orthopedic Surgery: Dr. Andriacchi is an associate professor and associate scientist, orthopedic surgery. He was the key person in the development of the Medical Center's John and Beatrice Keeshin Human Motion Laboratory. His work centering around the application of engineering principles to orthopedic problems has been highly productive and has resulted in broad recognition in the field of orthopedic surgery.

- James A. Schoenberger, M.D., the Charles J. and Margaret Roberts Professor of Preventive Medicine: Dr. Schoenberger is chairman of the Department of Preventive Medicine, and co-director, Rush Alzheimer's Disease Center. He is also president of the Rush medical staff. Dr. Schoenberger, a cardiologist, was president of the American Heart Association from 1980 to 1981 and served as one of the principal investigators in the Multiple Risk Factor Intervention Trial (MR. FIT), a seven-year study sponsored by the National Heart, Lung and Blood Institute of the National Institutes of Health.

- James H. Kimura, Ph.D., the CIBA-GEIGY Professor of Biochemistry: Dr. Kimura is an associate professor of biochemistry with a joint appointment in the departments of biochemistry and orthopedic surgery. Dr. Kimura, whose area of expertise is cartilage, is co-principal investigator of a five-year Congressionally mandated SCOR (Specialized Center of Research) grant of some $3.5 million to study arthritis. The author of some 50 scientific papers and book chapters, Dr. Kimura serves on the editorial board of the *Journal of Biological Chemistry.* D.W.

Name Two Department Heads

Lawrence H. Lanzl, Ph.D., director, Section of Medical Physics, Department of Therapeutic Radiology, has been elected chairman of the Department of Medical Physics. Dr. Lanzl helped launch the first medical physics master's program in the United States at The University of Chicago, and later its Ph.D. program. He is the president of the International Organization for Medical Physics, and past president of the American Association of Physicists in Medicine.

Rebecca Dowling, Ph.D., R.D., director, Food and Nutrition Services, has been elected chairman, Department of Clinical Nutrition. Dr. Dowling came to Rush in 1983 as assistant director of food and nutrition services. She was named director in 1986. Prior to joining the Medical Center, she was dietary department director at Westside Homes, Inc., in Nebraska.

Andreoli New Nursing Dean

Kathleen Gainor Andreoli, D.S.N., formerly vice president for educational services, interprofessional education and international programs at the University of Texas Health Science Center at Houston, is the new John L. and Helen Kellogg Dean of the College of Nursing of Rush University and the Medical Center's vice president for nursing affairs.

A native of New York, Dr. Andreoli earned her doctorate in nursing from the University of Alabama, Birmingham. She has lectured and written extensively on critical care nursing, particularly the care of coronary disease patients. She is co-author of *Comprehensive Cardiac Care*, (C.V. Mosby Co., St. Louis); has edited two books, and written over 45 book chapters, articles and reviews in her field.

Dr. Andreoli is a member of numerous professional and academic societies, including the Institute of Medicine of the National Academy of Sciences.

Program Aids Minority Students

Since 1979 Rush Medical College has trained medically and health-oriented college students in the Medical Center's clinical and research laboratories to give them hands-on experience with the human, research and technical aspects of medicine.

In this ongoing program, students are recruited in their senior year of high school by the Illinois Institute of Technology/Chicago Area Health and Medical Careers Program (CHAMPS). These students, whose academic averages are "B" or higher, attend weekly Saturday classes in mathematics, chemistry and communication skills at IIT, and spend one week visiting the Medical Center.

Rush Rounds

After completing their freshman year of college, the students return to Rush for a six-week summer orientation to medical school. "This session," explains Irene Turner, M.T., assistant professor, preventive medicine, the program coordinator, "places them in the basic science labs and as part of this program they report their experiences to other CHAMPS students."

In a new program initiated last year, the Medical Center and IIT went one step further, recruiting minority college students from around the country into an eight-week summer pre-entry program at Rush to teach would-be medical students how to maximize their chances of successfully applying to medical school and, if accepted, perform at their highest capabilities.

Rush provided the faculty; IIT provided program funds and student stipends.

The pre-entry curriculum concentrated on four major areas: anatomy/cell biology, physiology, organic chemistry/biochemistry and mathematics. Weekly exams in all courses evaluated students' progress and problem areas. Daily tutoring and counseling sessions stressed study skills as well as students' psychological and financial adjustments to medical school. Students who needed to improve their reading abilities received special help.

"All course curricula began at the undergraduate level, then quickly geared up to the medical school level to give the students a grounding in certain aspects of a true medical school course," explains Colin G.D. Morley, Ph.D., assistant dean, preclinical curriculum. "With an eight-week limit we couldn't cover everything so we took selected topics and studied them in depth."

Dr. Morley says the program "worked beautifully." A majority of the program's 23 students had previously applied to, and been rejected by, various medical schools, but after completing the pre-entry course, Dr. Morley was optimistic. "I expect the top six students to be in medical school within the year and another 12 to be accepted sometime in the future." (At press time, four students had been accepted to the Rush Medical College class of 1992.)

"Many of the students had poor undergraduate records because they worked full time while in school," Dr. Morley explains. "And because they were in their twenties, many still held 40-hour-per-week jobs. We told them that full-time work was impossible for medical students. We had to reorient their thinking."

For Catherine Wilbert, a University of Illinois graduate with a bachelor's degree in biology, the pre-entry program allowed her to assess her academic abilities free from the burden of work. "As a college student, I worked 40 hours but couldn't study much. I never knew why I did well in some areas and poorly in others and I didn't know how to improve my grades. I entered the Rush program to see how I could perform while not holding a job and I decided to use this experience as a basis for applying to medical school."

Mock interviews were an important component of the counseling sessions that were developed by Edward Eckenfels, the assistant dean of academic counseling, and his staff. All students practiced being interviewed as medical student applicants and critiqued their performances after watching themselves on videotape.

Wilbert, a pulmonary medicine research technician who unsuccessfully applied to Loyola Medical School in 1986, says the counseling sessions and mock interviews helped her subsequent job search and her medical school interviews. "My interviews have been much better because of my practice at Rush. "I learned how to answer interviewers' questions more specifically and how to clearly express my opinion."

Kimberly Meyer, currently auditing a biochemistry course at Rush, is determined to be in medical school some day. She believes the pre-entry program may help her get there. "I took the MCAT (Medical College Application Test) and found that the course material had really helped me. When I was interviewed at Rush my stress level was down a few notches because of the mock interview experience."

Meyer is thinking ahead, planning on earning a master's degree in public health if she is not accepted to medical school this year. But even after getting an M.P.H., she says she'll reapply to medical school. "Learning about glycolysis and the Krebs cycle in physiology and biochemistry and having someone put all the facts together was exciting."

Introducing students to the rigors of medical school early in their college years should help them make more informed and realistic career choices. For Meyer, the pre-entry program deepened her commitment to medicine. "It was a great program," she says. "I really want to be a doctor." J.F.

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Bruce Rattenbury, *Director of Public Relations*

Editorial Staff
Nancy K. Gallagher, *Editor*
Carmeline Esposito
Jane Friedman
Krys Kazieczko-Kuszak
Kerry Otto
Mary-Ann Redeker
Carolyn Reed
Debra Williams

Design: Leo A. Rotelli

Photography: David Joel

Cover illustration: Alan Camerer, Heidi Hoffer

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1653 West Congress Parkway
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